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CARCINOMA OF THE STOMACH

The Validity of Basing Prognosis upon Borrmann Typing or the Presence of Metastases

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IN this paper is presented an analysis, according to Borrmann's classification, of the relative influences of regional metastases and the gross anatomic types of gastric carcinomas on postoperative survival.

Schindler has recently offered evidence that the prognosis and perhaps the advisability of any therapeutic procedure for carcinoma of the stomach may be based upon the Borrmann type of the tumor. Borrmann separated the gastric carcinomas into 4 gross types: I, sharply demarcated polypoid carcinomas; II, sharply demarcated ulcerated carcinomas; III, partly infiltrating carcinomas; IV, diffusely infiltrating carcinomas. Combining types I and II as "limited" and types III and IV as "infiltrative" groups, Schindler noted that there was a much higher resectability rate and lower mortality rate for the former group. Of a series of 239 cases which he analyzed, resection was performed in 167. Exclusion of postoperative deaths and palliative resections left 107 resections for cure. Of this group, among those in which both the course and type of tumor were known, there were 7 three year cures (3 type I, 3 type II, and 1 type IV), and 4 five year cures (2 type I, 2 type II). It was concluded that the patient with a limited tumor has a 10 to 13 times greater chance of a three year cure than has the patient with an infiltrative tumor, and that for the latter no 5 year cure appears possible. On the basis of his data, Schindler questioned the advisability of resection of infiltrative tumors.

This view challenges the belief that as many carcinomas as possible should be resected and served as the stimulus for a review of the material at this clinic with special reference to Borrmann types of tumor. Another point, however, seemed to be of probable importance. It is obvious that survival is dependent on complete removal of the tumor and the likelihood of such removal should in the case of the stomach, just as for other organs, such as the breast, be to a degree reflected in the presence or absence of regional metastases. We have, consequently, compared the effects of the gross anatomic types of carcinoma and regional metastases upon the survival rates.

PRESENTATION OF DATA

In the period 1938-1943 inclusive the diagnosis of carcinoma was made in 342 individuals and gastric resection was performed on 177 of the group. The follow-up is complete

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TABLE I.—COURSE FOLLOWED BY 124 PATIENTS IN RELATION TO THE BORRMANN TYPES OF THE RESECTED CARCINOMAS

	Type I	Type II	Type III	Type IV	Total
Total cases	4 (3.2%)	35 (28.2%)	27 (21.8%)	58 (46.8%)	124
Postoperative deaths	0	6	6	12	24
Possible survivors	4	29	21	46	100
Failed to live 3 years	1	20	12	38	71
Lived 3 years	3	9	9	8	29
Lived 5 years	1	5	4	3	13
Alive June, 1947*	1	6	6	4	17

*Includes patients who have survived 3 years, but have not yet been exposed to a 5 year period

to June, 1947 in all cases. The data presented, however, concern only the 124 patients whose resected stomachs were available for re-examination and suitable for accurate determination of the Borrmann types of the tumors.

Although most tumors fall readily into the Borrmann types, here, as in other classifications, one must be arbitrary in some instances. We have been particularly critical of the determination of the limited tumors (types I and II). The extent of a tumor as determined by inspection of its surfaces and palpation is sometimes deceptive and we have also examined cut surfaces in order more accurately to segregate those tumors which presented a clearly defined advancing border. The several group designations concern only the manner of growth and have nothing to do with size. Thus, type IV tumors may range from small lesions apparently confined, but without demonstrable borders, in a small segment of the excised stomach to those which obviously infiltrate the entire organ. Those specimens which included direct extensions to adjacent organs such as liver or colon have been classified with respect to the character of the tumor and such direct extensions have not been classed as metastases.

The presence of metastases in lymph nodes was determined by routine methods of examination. In instances in which the original examination had failed to demonstrate involved nodes, the specimens were searched for further nodes, which, if found, were sectioned. For the purposes of this paper no distinctions are made relative to numbers of nodes involved, and they are considered simply as positive or negative for metastatic carcinoma.

For the 124 patients the distribution of the Borrmann types was as follows: 4 (3.2%) were of type I, 35 (28.2%) were of type II, 27 (21.8%) were of type III, and 58 (46.8%) were of type IV. Combining types I with II and III with IV, the series presents 39 (31.4%) "limited" tumors and 85 (68.6%) "infiltrating" tumors. This distribution approximates that found by Schindler in 87 cases where 34.5 per cent were limited, and 65.5 per cent were infiltrating.

Table I summarizes the course followed by the 124 patients with reference to the Borrmann types of their tumors. There were 24 postoperative deaths. For the limited tumors (types I and II) the mortality rate (6 of 39 patients) was 15.4 per cent. For the infiltrating tumors (types III and IV) the mortality rate (18 of 85 patients) was 21.2 per cent. One hundred patients survived resection and were discharged from the hospital. Their further course is shown in Table I and is summarized relative to both type of tumor and metastases in Table II. All of the deaths in this group have been due to recurrence of carcinoma. A few patients have lived 3 years but have not yet lived 5 years. They are included among those listed as living in June, 1947, in Tables I and II.

Of the 4 patients with type I tumors, 3 (2 without and 1 with metastases) survived 3

TABLE II.—COURSE FOLLOWED BY 100 PATIENTS WHO SURVIVED RESECTION IN RELATION TO BORRMANN TYPES OF CARCINOMAS AND THE PRESENCE OR ABSENCE OF METASTASES

Type	Nodes not involved				Nodes involved			
	Possible survivors	3 year survivors	5 year survivors	Alive* June, 1947	Possible survivors	3 year survivors	5 year survivors	Alive* June, 1947
I	2	2	1	1	2	1	0	0
II	8	5	4	4	21	4	1	2
III	4	4	1	2	17	5	3	4
IV	7	4	3	3	39	4	0	1
Total	21	15 (71.4%)	9	10	79	14 (17.7%)	4	7

*Includes patients who have survived 3 years, but have not yet been exposed to a 5 year period

years. One patient (without metastases) survived 5 years.

Twenty-nine of 35 patients with type II tumors survived resection and of this group, 20 (17 with demonstrable metastases) failed to live 3 years. Nine patients (5 without and 4 with metastases) survived 3 years. Five patients (4 without and 1 with metastases) survived 5 years. An additional patient (with metastases) was living and well in June, 1947, but had not yet survived 5 years.

Twenty-one of 27 patients with type III tumors survived resection and of this group 12 (all with metastases) failed to live 3 years. Nine patients (4 without and 5 with metastases) lived 3 years. Four patients (1 without and 3 with metastases) have survived 5 years. An additional 2 patients (one with and one without metastases) were living and well in June, 1947, but had not yet survived 5 years.

Forty-six of 58 patients with type IV tumors survived resection and of these 38 (3 without, 35 with metastases) failed to live 3 years. Eight patients (4 with, 4 without metastases) lived 3 years. Three (without metastases) lived 5 years. An additional patient (without metastases) was living and well in June, 1947, but had not yet survived 5 years.

From the data in Table I it may be seen that, combining types I and II as limited tumors and types III and IV as infiltrating tumors, among those patients who survived resection there are 33 limited and 67 infiltrating tumors. The 33 patients with limited tumors accounted for 12 of the 29 three year survivors, and 32 of them accounted for 6 of the 13 five year survivors. The 67 patients with infiltrating tumors provided 17 of the 29 three year survivors, and 64 of them provided 7 of the 13 five year survivors. Thus it is apparent that, although the patients with limited tumors make up the smaller group, they provide a proportionately larger share of the 3 and 5 year survivors. It may be seen in Table II that 21 patients, representing all Borrmann types, in whom metastases were not demonstrated, provided 15 three year survivors, and 20 patients without metastases provided 9 five year survivors. Of 79 patients with metastases 14 survived 3 years and, of 76 with metastases, 4 survived 5 years. The question is then raised whether it is the gross type of carcinoma which is crucial to survival or whether another variable related to the type of tumor, namely metastases, is more important. It is pertinent to know what each contributes to the total correlation with postoperative survival independent of the other variable.

The data have been subjected to statistical analysis. The material is not large enough to

TABLE III.—ASSOCIATION BETWEEN THE PRESENCE OR ABSENCE OF METASTASES AND POSTOPERATIVE SURVIVAL FOR PATIENTS WITH 3 YEAR FOLLOW-UPS (BORRMANN TYPE HELD CONSTANT)

A. Limited carcinomas (Borrmann types I and II)				B. Infiltrating carcinomas (Borrmann types III and IV)			
	Nodes				Nodes		
	Negative	Positive	Totals		Negative	Positive	Totals
Survivals	a=5	1		Survivals	a=8	9	
	t=1.9	4.1	6		t=2.8	14.2	17
	+3.1	−3.1			+5.2	−5.2	
Deaths	5	21		Deaths	3	47	
	8.1	17.9	26		8.2	41.8	50
	−3.1	+3.1			−5.2	+5.2	
Totals	10	22	32	Totals	11	56	67
Xi^2=	6.6	P(=)	.01	Xi^2=	12.7	P<	.001

TABLE IV.—ASSOCIATION BETWEEN THE PRESENCE OR ABSENCE OF METASTASES AND POSTOPERATIVE SURVIVAL FOR PATIENTS WITH A 5 YEAR FOLLOW-UP (BORRMANN TYPE HELD CONSTANT)

A. Limited carcinomas (Borrmann types I and II)				B. Infiltrating carcinomas (Borrmann types III and IV)			
	Nodes				Nodes		
	Negative	Positive	Totals		Negative	Positive	Totals
Survivals	a=5	1		Survivals	a=4	3	
	t=1.9	4.1	6		t=1.1	5.9	7
	+3.1	−3.1			+2.9	−2.9	
Deaths	5	21		Deaths	6	51	
	8.1	17.9	26		8.9	48.1	57
	−3.1	+3.1			−2.9	+2.9	
Totals	10	22	32	Totals	10	54	64
Xi^2=	6.6	P(=)	.01	Xi^2=	4.1	P<	.01

TABLE V.—RELATIONSHIP OF BORRMANN TYPE TO POSTOPERATIVE SURVIVAL FOR PATIENTS WITH A 3 YEAR FOLLOW-UP (PRESENCE OR ABSENCE OF METASTASES HELD CONSTANT)

A. Nodes negative				B. Nodes positive			
	Borrmann types				*Borrmann types*		
	Limited	Infiltrating	Totals		Limited	Infiltrating	Totals
Survivals	a=7	8		Survivals	a=5	9	
	t=7.1	7.9	15		t=4.1	9.9	14
	−0.1	+0.1			+0.9	−0.9	
Deaths	3	3		Deaths	18	47	
	2.9	3.1	6		18.9	46.1	65
	+0.1	−0.1			−0.9	+0.9	
Totals	10	11	21	Totals	23	56	79
				X^2=	0.7	P=	0.8

TABLE VI.—RELATIONSHIP OF BORRMANN TYPE OF CARCINOMA TO POSTOPERATIVE SURVIVAL FOR PATIENTS WITH A 5 YEAR FOLLOW-UP (PRESENCE OR ABSENCE OF METASTASES HELD CONSTANT)

A. Nodes negative				B. Nodes positive			
	Borrmann types				*Borrmann types*		
	Limited	Infiltrating	Totals		Limited	Infiltrating	Totals
Survivals	a=5	4		Survivals	a=1	3	
	t=4.5	4.5	9		t=1.2	2.8	4
	+0.5	−0.5			−0.2	+0.2	
Deaths	5	6		Deaths	21	51	
	5.5	5.5	11		20.8	51.2	72
	−0.5	+0.5			+0.2	−0.2	
Totals	10	10	20	Totals	22	54	76

Closest possible agreement—Xi^2 not calculated

permit segregation into each of the four Borrmann types without raising serious statistical problems relative to small numbers. Therefore, the types were grouped as indicated into limited and infiltrating tumors. The 100 patients who survived resection were divided accordingly and within each group the determination of the relationship of metastases to 3 year survival is freed of the influence of the Borrmann type since the latter variable is held constant. Likewise the relationship between Borrmann type and survival was determined by dividing the patients into 2 groups representing those with and those without metastases, thus holding the latter variable constant. The 5 year survival rates were similarly considered for the 96 patients concerned.

The relationship of metastases to survival, freed of the influence of the Borrmann types, is shown in Tables III and IV for 3 and 5 year survivals, respectively. The first entry in each basic cell of the tables defines the actual frequency, *a*. The next specifies the theoretical number, *t*, of cases to be expected in each cell if no relationship exists between metastases and survival. The remaining entry is the deviation of the actual frequency from the theoretical, alike in number in all 4 cells but differing in sign.

The data of Table III show that, among 33 patients with limited tumors, 7 of 10 without metastases, and 5 of 23 with metastases survived 3 years, and that, among 67 patients with infiltrating tumors, 8 of 11 without metastases, and 9 of 56 with metastases survived 3 years. Table IV shows that among 32 patients with limited tumors, 5 of 10 without metastases and 1 of 22 with metastases survived 5 years, and that among 64 patients with infiltrating tumors, 4 of 10 without metastases and 3 of 54 with metastases survived 5 years.

The association between survival and metastases is definite within both groups of carcinomas. In each of the tabulations (panels A and B of Tables III and IV) more patients died when metastases were demonstrated and more lived when metastases were not found than should theoretically be expected if metastases did not affect the probability of 3 or 5 year survival. It is clear that these differences are not chance deviations because the Xi^2 criterion shows each, considered alone, to be significant[1]. Taken collectively there is no reason to doubt that the association is real. The Xi^2 values for the two panels of Table III may be combined, giving a *P* of considerably less than 1 in a thousand. Similarly the two panels may be combined in Table IV where it is found that *P* lies between 1 and 2 per thousand.

[1] A probability of less than 5 per cent that each set of 4 differences would arise through chance alone is considered here as significant. This conforms to standard practice in statistical analysis.

The relationship of the Borrmann types to survival, considered independent of the presence or absence of metastases, is shown in Tables V and VI, for 3 year and 5 year survivals respectively. Among 21 patients without metastases 7 of 10 with limited tumors and 8 of 11 with infiltrating tumors survived 3 years. Of 79 patients with metastases 5 of 23 with limited tumors and 9 of 56 with infiltrating tumors survived 3 years. Among 20 patients without metastases 5 of 10 with limited tumors and 4 of 10 with infiltrating tumors survived 5 years. Among 76 patients with metastases 1 of 22 with limited tumors and 3 of 54 with infiltrating tumors survived 5 years.

In each of the cells of Tables V and VI, the actual frequency deviated from the theoretical (based on no association) by less than unity and in 3 of 4 tabulations (panels A and B of Table V and panel A of Table VI), the agreement with expectation is as close as it can be since observed frequencies must be whole numbers. The one tabulation (Table VI, B) in which a statistical test for real discordance has some meaning yields a probability that such discrepancies or worse would arise by chance approximately 4 times out of 5 (P is 0.8, approximately). It is therefore demonstrated that when the presence or absence of metastases is ignored, the Borrmann classification owes its relationship to postoperative survival solely to the fact that the infiltrating forms have a higher probability of metastases.

COMMENT

Schindler suggested that, in view of the poor prognosis in patients with infiltrating tumors, the combined use of gastroscopy and x-ray might serve to separate patients with limited tumors as the more likely candidates for surgery. His contention, however, that clinical determination of the Borrmann type might form the primary basis of decision as to operative interference seems now to rest on the correlation between the gross types and the presence of metastases. Tables I and II show that the correlation is not perfect. Of 67 patients with infiltrating tumors 17 survived at least 3 years and 8 of the 17 showed no metastases. Of 33 patients with limited tumors, 21 failed to live 3 years and of these, 18 had metastases. The Borrmann types alone, then, even when determined postoperatively, prove to be inadequate indicators of the wisdom of surgical procedures. On the other hand we find that there is the probability of survival for a period of 3 years in approximately 70 per cent (15 of 21 patients) of those cases in which metastases are not found, but that the probability falls to about one-quarter of that figure when metastases are demonstrated (17 of 79 patients).

The examination employed for determination of metastases is relatively crude. Sample sections of nodes undoubtedly miss some small metastases; some small nodes are not found, and there is in addition no certainty, for any given specimen, that all tumor-bearing nodes have been removed. However, the data indicate that for gastric carcinoma, as for carcinoma elsewhere in the body, the likelihood of complete removal of tumor-bearing tissue is reflected to a high degree in the determination, even by routine methods, of the presence or absence of metastatic tumor in the regional lymph nodes.

To the extent that the infiltrating tumors are less readily excised without leaving microscopic extensions in the gastric wall and more likely to have metastasized, they offer a poor prognosis compared to the limited tumors. However, in some patients infiltrating tumors are confined to excised tissue to a degree consistent with long survival. The limited tumors offer a better prognosis only when lymph nodes are not involved and the presence or absence of metastases cannot be determined preoperatively. To restrict surgical excision to those patients with limited tumors would deprive some patients, though admittedly few, with infiltrating tumors of the chance for long survival and many more of palliation with reasonable comfort for periods averaging up to 2 years (State, Moore, and Wangensteen). Without therapy most patients live but a few months after the diagnosis is established. In view of the low risk and short convalescence accompanying gastric resection, it would appear difficult to argue that the opportunity of over 22 months of relative comfort and the chance of longer survival should be withheld from any patient.

Thus, it would seem that attempts to predict the survival of patients with carcinoma of the stomach by the gastroscopic typing of their lesions are not justified. If patients with Borrmann types III and IV are denied operation, a certain number of lives will be needlessly lost. It has been shown that these patients do have a reasonable chance of survival if no metastases are present.

It may further be noted that the kind of data upon which this study is based has now been improved. In 1945 the operability rate for carcinoma of the stomach at this clinic was 89 per cent, resectability 79.6 per cent and the mortality rate 4.8 per cent. In addition, the recent introduction of the thoracoabdominal approach has increased the chances of removing infiltrating and high lying lesions as well as metastases. In the last 16 total gastrectomies at this clinic, there has been but one death. These techniques should favorably influence the removal of infiltrating lesions, and contribute to longer survival.

CONCLUSIONS

1. The presence or absence of demonstrable metastases in regional nodes among patients subjected to gastric resection for carcinoma has a greater prognostic value than does the Borrmann type of the tumor.

2. The Borrmann type affects the prognosis of groups of cases to the extent that the limited tumors provide a proportionately large number of patients free of metastases while the infiltrating tumors which are more numerous are more likely to have metastasized.

3. The presence or absence of metastases cannot be accurately determined preoperatively and no patient should be denied operation because of the type of tumor he may be determined to have.

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THE FIVE YEAR SURVIVAL RATE IN CASES OF COMPLETELY OBSTRUCTING ANNULAR CARCINOMA OF THE DESCENDING COLON AND SIGMOID

A Pathologic Study

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OBSTRUCTION superimposed on an existing malignant lesion of the colon is a serious complication. Long before 1810 when Thomas Copeland described stenosing carcinoma of the colon, many procedures, beginning with the decompression colostomy first performed by Littre in 1710, had been devised for relief of this condition. By 1839 Amussat, the French surgeon, was performing decompression colostomy on both the right and left halves of the colon. Later attempts were made to extirpate the malignant lesion. Kohler in 1881 reported the first successful resection. Mikulicz, in 1903, described his exteriorization procedure and reported a mortality rate of 12.5 per cent in 16 cases. Miles, at the turn of the century, favored the combined abdominoperineal approach. In every procedure, however, obstruction continued to plague the surgeon, keeping his operative mortality uncomfortably high. With the advent of chemotherapy there is little doubt that the mortality rate has been revised downward. But what of the 5 year survival in cases in which obstruction complicates the presence of colonic carcinoma?

We have felt for some time that obstruction itself in some way decreases the expected 5 year survival rate. A review of the literature offered little actual statistical support of this hypothesis. However, 5 important points were brought out which were conceded to be contributing factors. (1) Damage to the bowel wall by the increased intraenteric pressure has been reviewed and studied by many men (2, 14–18) who have shown that permeability of the wall of the obstructed colon is increased and that lymphatic absorption appears to be increased. We believe that this may also facilitate earlier metastasis of carcinoma cells. (2) The inflammatory swelling, distention, engorgement of vessels and edema of the intestinal wall and of the carcinoma itself probably tend to break down any protective forces (3, 8, 10, 11) brought into operation by the tissues of the host. (3) The increasing hypertrophy of the musculature of the colon and the attempts by the bowel to force fecal material through an increasingly smaller aperture may result in traumatizing and vigorous massaging of the tumor (7, 8) which may induce earlier and more widespread metastasis. (4) The motility of cancer cells is of debatable significance, but such motility was demonstrated by Cormalt in 1872 and again later (8, 9). Also there exists the possibility of the elaboration by carcinoma cells of some lytic or other damaging property which enables malignant cells to break through the basement membrane and invade the deeper tissues. Whatever this invasive property might be, the intestinal wall damaged by obstruction would offer an easier pathway of extension. (5) The ileocecal valve, when competent, produces a closed loop type of obstruction. Whether it is done by valve or sphincter action, the relatively low intraenteric pressure produced, if it is exerted for 27 to 32 hours, will destroy the viability of the bowel or definitely impair its normal function (18). The aforementioned changes in the wall are accentuated.

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FACTORS CONTRIBUTING TO THE OBSTRUCTION

Gruenfeld listed 4 factors contributing to the development of colonic obstruction; namely: (1) inflammatory edema, (2) impaction of solid feces, (3) kinking of the bowel with varying degrees of intussusception, and

(4) fatigue of the intestinal muscle above the point of stenosis. Rankin considered 3 factors in reference to the left versus the right portions; namely: (1) the character of the intestinal wall itself which is less elastic, and smaller in diameter than its fellow in the right half; (2) the fecal current which is formed and hard in contradistinction to the liquid stream of the right side, and (3) the pathologic characteristics of the growth which in lesions of the left portion of the colon has a tendency to encircle the lumen and thus bring about slow stenosis. From our study of the size of the obstructing annular lesions as compared to similar nonobstructing lesions, we would conclude, as others have, that the obstruction is dependent, too, on the amount of fibrosis present, a reaction on the part of the host to the presence of cancer cells.

PURPOSE OF STUDY, MATERIAL, AND METHODS

Purpose. We have often noted in the operating room and in the surgical pathology laboratory that at the time of the initial exploration involvement of the regional nodes or metastasis to the liver, frequently is associated with small but obstructing carcinomas of the left part of the colon. We have observed, too, that patients who have undergone resections for "favorable" lesions of small size often returned in from 1 to 3 years because of unmistakable signs or symptoms of metastatic carcinoma. We, therefore, considered examination of the factor of obstruction as pertinent in the 5 year survival rate of patients who had obstructing annular carcinoma of the left portion of the colon.

Material. Two hundred and fifty-four cases of carcinoma of the left portion of the colon in which operation had been performed in the 36 years, 1910 through 1945 and in which obstruction was present, were reviewed. All cases were discarded except those in which complete clinical obstruction was present and for which cecostomy or colostomy was required for decompression. All lesions of polypoid type were discarded. All cases of carcinoma occurring at or below the peritoneal fold and at the splenic flexure were eliminated in order that we might determine the reaction of the bowel to the obstruction, both as to the percentage increase in the circumference of the lumen above the carcinoma, and to the percentage increase in the thickness of the muscularis propria above the lesion. The final group studied consisted of 78 cases of completely obstructing annular carcinoma of the sigmoid and descending colon. In 55 of these the lesions occurred in the sigmoid and in 23 in the descending colon. All lesions had been removed surgically and the specimens had been preserved in 10 per cent commercial formalin (40 per cent formaldehyde). For comparison, all cases of surgically removed, nonobstructing carcinomas of the descending colon and sigmoid encountered at the Mayo Clinic in 10 years, 1930 through 1939, were studied; again all cases of polypoid type were excluded. This control group totaled 329 cases.

In order to determine the incidence reference is made to the total of 2,089 cases of carcinoma of the descending colon and sigmoid in which operation was performed at the clinic during the 36 years covered by the detailed study.

Methods. Gross pathologic studies were carried out on each specimen to ascertain that it was in fact completely occluding the lumen of the bowel and that it was an annular or napkin-ring type. Each carcinoma was carefully measured in three dimensions to determine the cubic content of tumor tissue. The circumference of the lumen and the thickness of the muscularis propria were measured proximal and distal to the carcinoma to the nearest 0.5 millimeter and charted. Blocks of tissue then were cut from the proximal and distal edges of the tumor and at the peritoneal surface for grading (Broders) and classification by Dukes' method. A careful search was made for involved nodes and each was sectioned for study. All specimens were placed in fresh 10 per cent solution of formalin and later studied under the microscope in paraffin sections stained with hematoxylin and eosin.

INCIDENCE, AGE, AND SEX

Annular carcinomas comprise 60 to 70 per cent of all carcinomas of the colon encountered clinically and require, in an average case, about 2 years to encircle the bowel completely

TABLE I.—OBSTRUCTING AND NONOBSTRUCTING CARCINOMA* OF THE DESCENDING COLON AND SIGMOID: A COMPARISON OF THE GRADE OF MALIGNANCY

Grade	Nonobstructing		Obstructing	
	Cases	Per cent	Cases	Per cent
1	34	10.3	10	12.8
2	249	75.7	56	71.8
3	38	11.6	10	12.8
4	8	2.4	2	2.6
Total	329	100.0	78	100.0

*Polypoid lesions, a large percentage of which are grade 1, are not included in this series.

TABLE II.—FIVE YEAR SURVIVAL RATE ACCORDING TO DUKES' CLASSIFICATION AND BRODERS' GRADING

Dukes' classification	Traced patients	Lived 5 or more years		Broders' grade	Traced patients	Lived 5 or more years	
		Number	Per cent			Number	Per cent
A	11	4	36.4	1	2	1	50.0
B	9	2	22.2	2	25	7	28.0
C	15	3	20.0	3	7	1	14.3
				4	1	0	—
Total	35	9	25.7		35	9	25.7

(4). Nevertheless, obstructive phenomena dominate the clinical picture of carcinoma of the left part of the colon with 75 to 80 per cent of patients having obstructive symptoms at the time they first consult a surgeon (1, 5, 12, 13). A higher percentage give roentgenologic evidence of obstruction and about half of these patients have colicky pain (1). Obstruction is usually a late sign of malignant growth of the colon which occurs as a slowly progressive process. About 5 per cent of patients, however, will have signs of acute obstruction as the first symptom (13, 14). In our series, 2,089 patients with carcinoma of the sigmoid and descending colon have been operated on. In 254, an incidence of 12.2 per cent, acute or subacute obstruction, grade 1 to 4 (grade 4 represents complete obstruction) was found. Complete obstruction was present in 78 cases, an incidence of 3.7 per cent for the entire group, and 30.7 per cent for the group in which some degree of obstruction was encountered. Therefore, in about a third of cases in which obstruction was present, complete obstruction had occurred before the surgeon saw the patient.

There were 41 women and 37 men in this series. The number of women in the younger age groups was somewhat greater than of men.

PATHOLOGIC DATA

Size. It is generally agreed that there is little correlation between the size of a malignant colonic lesion and the degree of obstruction present. In our series of 78 cases, however, paradoxically enough, the cubic contents of the lesions which produced obstruction averaged 40 cubic centimeters as against 64 cubic centimeters for those which were not obstructive (control series).

Grade. Apparently the grade of the lesion and the incidence of obstruction are not related (Table I). Although our series of cases is small, the incidence of the obstructing and nonobstructing lesions of various grades of malignancy is similar. The 5 year survival rates in cases graded by the Broders' method and also classified by Dukes' method are recorded in Table II. We do not intend to imply that Dukes' classification is not of value, for we know that it is in other and larger series. However, the statistics in this series indicate that obstruction in some way materially alters the 5 year expectancy as "predicted" by Dukes' method of classification.

Hypertrophy and dilatation. Seven specimens could not be accurately studied from the standpoint of hypertrophy and dilatation. Two were gangrenous, and 5 had been subjected to exteriorization and were so distorted that accurate measurement was impossible. In the remainder we found the mean thickness of the muscularis propria above the lesions to be exactly double that of the mean thickness below the lesions (2.66 and 1.33 mm., respectively) and the circumference of the lumen above the lesions to be approximately double that of the circumference below the lesions (7.93 and 4.50 cm., respectively). All of these specimens had been preserved in formaldehyde and it is probable that there was a greater percentage of shrinkage in the proximal edematous part of the bowel than of the more normal distal part and that the actual

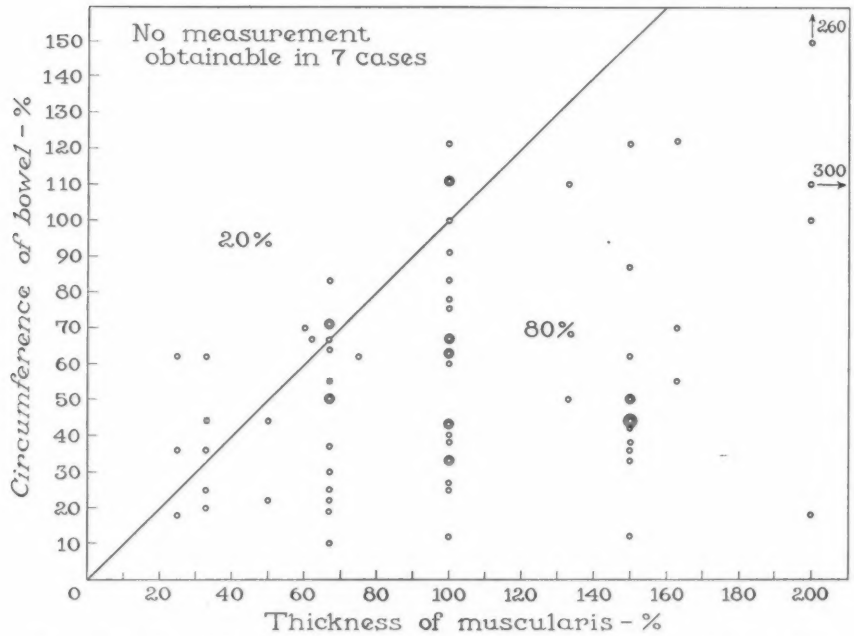

Fig. 1. Comparison of increase in size of lumen to increase in size of muscularis above the obstructing carcinoma.

percentage increase in the luminal circumference was greater than that shown, and that there was a similar but less striking difference in the muscularis propria.

In approximately 80 per cent of cases the percentage increase in the size of the muscularis propria above the tumor was greater than the percentage increase in the size of the lumen, whereas in approximately 20 per cent the percentage increase in the size of the lumen of the bowel was greater (Fig. 1). One might think that this 20 per cent represents cases in which obstruction was of short duration. However, in 3 of the cases (about 20 per cent) in which the increased dilatation was greatest, obstruction had been present for only 1 day before surgery, in 5 for 7 to 14 days, and in 4 between 2 and 5 days.

RELATION OF DAYS OF OBSTRUCTION TO THE SURVIVAL RATE

The relationship of the duration of obstruction in days before operation to the survival rate was investigated. The duration of obstruction was taken from the records and in some cases only an approximation could be made. No relation between duration of obstruction and length of survival is evident. It was somewhat of a surprise to see that 4 of the 9 patients who lived 5 years after operation had had obstruction for 7 days to 2 weeks before operation. We expected to find a higher incidence of 5 year survivals in cases of obstruction of short duration, but our data do not substantiate this impression. One explanation may be that complete obstruction occurred early in these cases and that impairment of the mesenteric circulation and decreased intestinal activity eliminated the factor of massage; or an incompetent ileocecal valve prevented a closed-loop type of obstruction, with minimal damage of intestinal wall.

THE FIVE YEAR SURVIVAL RATE

Of the 78 patients who had completely obstructing annular carcinoma of the descending

TABLE III.—SURVIVAL RATES FOR THREE AND FIVE YEARS IN CASES OF OBSTRUCTING AND NONOBSTRUCTING ANNULAR CARCINOMA OF THE DESCENDING COLON AND SIGMOID*

Group	Survived 3 years				Survived 5 years			
	Patients		Lived 3 years or more		Patients		Lived 5 years or more	
	Total	Traced	Number	Per cent	Total	Traced	Number	Per cent
Nonobstructing lesion†	329	328	208	63.4	329	321	166	51.7
Obstructing lesion‡	47	43	22	51.1	37	35	9	25.7

*Hospital deaths not included in this series.
†All patients who had resections of the colon for nonobstructing ulcerative adenocarcinoma at the clinic from 1930 to 1939 inclusive are included.
‡All patients who had resections of the colon for obstructing adenocarcinoma of the descending colon or sigmoid at the clinic in 1939 or earlier are included for the determination of the 5 year survival rates and those who had them in 1941 or earlier for the determinations of the 3 year survival rates

colon and sigmoid, 39 were seen in 1939 or earlier. Since the follow-up for survival was as of January 1, 1945, these were used to determine the 5 year survival rate (Table III). Data on the 2 patients who died in the hospital were not included in Table III. Of the 37 remaining patients 2 could not be traced for 5 years after operation. The 3 year survival rates also are shown. However, these are not of great significance for this period of survival might be expected after palliative surgery. Such is not true for the 5 year group. A comparison of the 5 year survival rate with that in cases of nonobstructing annular type of lesion shows that for completely obstructing annular carcinoma of the descending colon and sigmoid the rate is approximately half that for the nonobstructing annular type of carcinoma. The 5 year survival rate in the cases of nonobstructing annular carcinoma of the descending colon and sigmoid was 51.7 per cent and that in cases of completely obstructing annular carcinoma was 25.7 per cent.

SUMMARY AND CONCLUSIONS

The 5 year survival rate in 37 cases of completely obstructing annular carcinoma of the descending colon and sigmoid in which resection was performed is compared with the 5 year survival rate in cases in which nonobstructing lesions had been treated surgically. These rates were 25.7 per cent and 51.7 per cent, respectively.

The five factors which may contribute to the lowered 5 year survival rate are: (1) damage to the intestinal wall with increased permeability and increased lymphatic absorption; (2) hypertrophy of the musculature which produces a massaging and traumatizing action to the carcinoma at the site of obstruction; (3) inflammatory swelling and edema which cause breakdown of any mechanical protective factor, and of any protective forces elaborated by the host; (4) the invasive property of the cancer cell, whether it be motility or some lytic action, which is facilitated by the effect of the factors just mentioned, and (5) the ileocecal valve which may produce a closed-loop type of obstruction.

The size of the lesion is of no significance in prognosticating the presence of metastasis, and the volume (cubic centimeters) of malignant tissue is actually less in the cases of obstruction than in the cases in which no obstruction was present.

No correlation was found between the grade of the lesion and the incidence and degree of obstruction or between the duration of obstruction in days and the survival rate.

We realize, of course, that this is a small series of cases on which to base any definitive conclusions, but with the strict criteria for obstruction used, namely, complete obstruction requiring a colostomy or cecostomy for decompression before removal of the lesion, the series would of necessity have to be small. Notwithstanding, we do believe that such a difference in the 5 year survival rate in cases of obstructing and nonobstructing carcinoma of the descending colon and sigmoid, 26 per cent in this series, is significant. This difference is not due to a difference in the grade of malignancy of obstructing carcinomas but rather apparently to the condition of the intestinal wall attending the complication of obstruction.

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COMEDOMASTITIS

A Clinical and Pathologic Study of Data in 172 Cases

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COMEDOMASTITIS is a disease of the breast characterized by dilatation of the lactiferous ducts which are distended with inspissated grumous material that may be expressed from the cut ends of the ducts much as comedones are expressed from ordinary blackheads. It is a disease of the large ducts in contrast to chronic cystic mastitis which is a disease of the acini and ductules. Marked clinical similarity to mammary malignancy may be present when comedomastitis results in an indurated area of the breast which is fixed to the skin and is associated with a retracted nipple. Even the pathologic picture may be confused with that of carcinoma unless the true nature of the lesion is appreciated.

REVIEW OF LITERATURE

The use of the term "comedomastitis" to describe this condition has gained limited acceptance (15, 19, 45, 57). Dilatation of the ducts has long been known to exist in chronic cystic mastitis and senile atrophy of the breast but Bloodgood (6–10) was the first to consider this type of lesion as a clinical and pathologic entity which he called "varicocele tumor of the breast." He noted that the condition was usually bilateral and that it was more common in women more than 45 years of age. Parity appeared to have little influence on the frequency of occurrence. He described dilated thick walled ducts which contained green, brown, milky or creamlike material of varying degrees of viscosity and consistency. Sometimes induration was so marked that the lesion looked, felt, and cut like carcinomatous tissue. He found the lesion in breasts that were otherwise normal, senile, adenomatous, cystic, or malignant. However, he stated that the gross finding of ducts distended with grumous material militated against a diagnosis of mammary carcinoma.

Cheatle (12), and Cheatle and Cutler (14) expressed a belief that enlargement of ducts resulted from overgrowth of epithelium and excessive desquamation rather than from obstruction. They described (13, 14) conditions clinically similar to comedomastitis and saw dilated ducts with retained secretion in carcinomatous breasts. Adair and Bagg indicated that abnormal drainage from the breast was an important factor in production of cancer. Adair (2) found obstruction which was due to a localized growth of the lining epithelium of the ductules; to abnormality of the nipple, including inversion, bivalving, puckering, adherence, dwarfing and ulceration; to fibrous scars across the lumina of ducts; to cysts, fibroadenoma or inflammation; to desiccated, desquamated cells; or to epithelial debris that plugged the ductal estuaries. Semb found dilatation of the milk ducts in association with fibroadenomatosis which he stated predisposed to bacterial infection, but he could demonstrate no connection between the occurrence of local purulent inflammation and the development of cancer. Handley described "duct catarrh" wherein plugs of epithelial debris marked the orifices of the milk ducts from which wormlike casts of material could be clinically expressed. There was thickening of the ducts as they converged on the nipple.

In breasts with cystic disease, Lewis and Geschickter found ectasia of the ducts, which sometimes were filled with material of puttylike consistency. They attributed cystic disease to hormonal imbalance and observed that theelin produced similar changes in animals. Later, Geschickter described 72 cases in which

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there was dilatation of mammary ducts beneath the nipple and he expressed a belief that the condition represented a senile involutionary change occurring especially in parous women at or near the menopause. His patients usually gave a history of swelling, pain, itching or redness in the region of the nipple associated with a sticky or grumous discharge from the nipple. The condition was bilateral in 32 cases. Doughy, wormlike masses were felt beneath the nipple and induration and retraction simulating that of cancer was sometimes present. One or more large ducts were distended to diameters up to 1.5 centimeters. The retained material was often composed almost entirely of desquamated cells with pale, foamy cytoplasm and small dense nuclei. In some the material consisted of amorphous, inspissated secretion. The walls of involved ducts were lined by several layers of cells, with the innermost being secretory or occasionally undergoing desquamation. About the enlarged ducts there were aggregates of wandering cells, with lymphocytes and plasma cells predominating. The amount of inflammation varied with the amount of infection and with the amount of "decomposition" of the inspissated material. The disease usually disappeared spontaneously and most of his patients were treated conservatively, 32 recovering without operation.

Taylor (52, 53), and Taylor and Waltman listed disease of the breast in association with discharge from the nipple as one of the entities included in the term "chronic cystic mastitis." On examination, the breast was normal, indurated, or diffusely nodular. The basic change found was dilatation of the larger ducts, which were filled with amorphous secretion, usually thick or semisolid. As a rule, the lining cells were flattened although sometimes larger pale cells with round nuclei were seen. Evidence of marked epithelial proliferation and even papillomas were occasionally present. There was usually a zone of periductal inflammation and sometimes necrosis and abscess formation. The lobules were normal, small and insignificant, or large and numerous. The patients averaged 35 to 36 years of age and more than 80 per cent had had children. Disturbances of the menstrual cycle were common and the average daily secretion of estrin was low. About half of the patients had some pelvic abnormality.

Lepper and Weaver reported 8 cases in which generalized distention of the ducts of the breast by fatty secretion occurred in single and married women, parous and nonparous. Some of the ducts might have been plugged by collections of epithelial cells but others were not, and all were equally distended. Ingleby described "secretory cystic disease" caused by abnormal hormonal stimulation wherein the ducts were dilated and filled with inspissated material.

Foote and Stewart reported a lesion complex characterized by ductal stasis, ductal dilatation, and periductal "mastitis" that occurred in benign and malignant conditions of the breasts. The average age for the benign conditions was 41.7 years and for the malignant conditions, 49.7 years. In the older age groups the changes were more likely to be diffuse and to be related to the changes of senile atrophy. Lactation did not seem to play a part in the pathogenesis. Minor degrees of epithelial piling up and loosening were fairly common when the stasis and distention were slight. An almost invariable finding was that of flattening and atrophy of the epithelium at the sites of marked distention and periductal mastitis. Blood pigment was sometimes found and fat-laden phagocytes were common within the the ducts. Erosions of the epithelial lining occasionally occurred, and where the wall of the duct was weakened or had been penetrated and the contents of the duct had gained access to adjacent fatty tissue, a process characterized by fat necrosis developed. Anatomic obstruction was not considered necessary for production of the complex but pressure from papillomas, cysts and other tumors, along with senile dilatation of the ducts, was considered as facilitating the process. In many cases there was no obvious explanation. The lobules distal to a site of involvement showed changes tending toward atrophy. Cysts or hyperplasia, when present, never appeared to begin as a result of periductal mastitis or stasis. No atypical cytologic changes were noted in the atrophic or hyperplastic epithelial lining in the regions of stasis, distention or periductal mas-

titis, and in none of the cases of "cancer" could the source of the growth be traced to the "comedomastitis." They concluded that the lesion complex was not primarily related to the proliferative and cystic lesions but that it might occur independently or in unison with the others.

Other authors have reported or described cases similar to those of comedomastitis (5, 11, 16, 21–23, 28, 29, 32, 35, 40, 42–44, 49, 51, 55, 57, 58). It has been shown that those breasts which have produced large quantities of milk have larger ducts than poorly secreting or non-secreting glands (31). The effects of hormones on the breasts of animals have been summarized by Patey and Shimkin.

MATERIAL AND METHOD

The surgical and pathologic files of the Mayo Clinic were searched for the records of all cases in which the diagnosis of comedomastitis had been made for the years 1925 through 1942. Material which had been taken at mastectomy in 185 cases and at local mammary resection for comedomastitis in 19 cases and which had been preserved in 10 per cent solution of formalin was secured and studied. In cases in which bilateral mastectomy had been done with a different diagnosis for the lesions in the 2 breasts, the "uninvolved" breast still was reviewed with the idea of picking up minimal or early "comedo" changes. Size and distribution of the ducts were particularly noted although cysts, abscesses, fibrosis, fibroadenoma, carcinoma and papilloma were also looked for. Ducts were often probed or laid open to be certain of their true character. As a rule, one block from each quadrant and one through the nipple of each of the whole breasts was taken, so as to demonstrate typical areas of comedomastitis, minimal areas and transition zones. When only a portion of the gland was available, one piece was chosen to show the typical pathologic picture. All blocks were placed in a fresh 10 per cent solution of formalin and slides were subsequently prepared by the freezing method and stained with hematoxylin and eosin.

For a better understanding of the condition, those cases in which operation was performed solely for the relief of comedomastitis were considered separately from the group wherein the main diagnosis was carcinoma or papilloma. The first group was represented by material from 144 whole breasts and 19 incomplete breasts; in the second group material from 41 cases in which mastectomy had been performed was available for study.

PATHOLOGIC CONSIDERATIONS

The size of the involved breasts varied from enormous, fatty glands to shrivelled nubbins. The nipple was available for study in 143 breasts; it was abnormal in 31 breasts, with retraction or inversion in 28 and inflammation in 3. In 1 case, the nipple had been surgically removed previously. Fifty-five contained palpable single masses and 16 multiple masses. Fifty-nine breasts were described as diffusely nodular, granular, cystic or shotty, and 23 had localized thickening or nodularity. In only 2 were the dilated ducts noted as being palpable. Fixation of the mass to the skin, or to the nipple, was present 37 times. In 1, a draining sinus was present. In 5, abscesses were identified. Eight contained nodules typical of fibroadenoma and 1 contained a lesion which later proved to be fibrosarcoma. As this seemed to be entirely unrelated to the mastitis the case was included in the benign series.

After section of the gland, the most striking feature noted was the presence of comedones which could be squeezed from the ducts like toothpaste from a tube. Although typically grumous, this material varied from an oily secretion to a thick dry form with the consistency of cheese (Fig. 1). The color was white, gray, yellow, green, or brown. Many of the ducts were large and thick walled so that they stood out like pipestems, even after the secretion was expressed, but some would collapse to slits. The extent of the ectasia varied from indistinct enlargements in scattered sites to markedly dilated cavities that honeycombed the gland. In 29 of the specimens only slight dilatation occurred. In the 96 in which moderate degrees of ectasia occurred, in 8 the ectasia was in scattered parts, in 27 it occurred beyond the nipple only and in 61 it occurred diffusely. In 19 breasts there were marked changes, with large ducts running from the ampulla to the periphery in all sectors. Six of

the excised portions of mammary tissue exhibited minimal, 11 moderate and 2 marked dilatation.

Fibrosis was obvious in the atrophic type of breast in which sections were sometimes difficult to cut. In the fatty organs, this was still evidenced by the increased density of the septa. Eighty-seven of the specimens contained macroscopic cysts varying from a minimum of 1 millimeter to 8 centimeters across.

The prominent and distinguishing features of the microscopic structure were the changes in the ducts and periductal tissues. The method of preparation frequently destroyed the retained secretion, but where the secretion did persist, it consisted of pink-staining amorphous, granular, or cellular debris. At times, fat-laden phagocytes, inflammatory cells, and desquamated epithelial cells were found within the lumen. The distribution and degree of dilatation of the ducts, as seen microscopically, was, for the most part, as indicated in the description of the gross appearance, but differences did occur. Even when the ducts seemed diffusely distended, a few usually remained almost normal in size and contour. In the most marked cases, all ducts seen near the nipple were enlarged (Fig. 2). Some of those that were grossly affected only near the nipple or in scattered areas exhibited microscopic changes in the ductal and periductal tissues indicating diffuse disease. For the most part, the ducts near the nipple were irregular in outline and somewhat collapsed when the retained secretion was lost, but many of the peripheral ducts remained wide open as a result of fibrosis.

Aside from round cell infiltration associated with the lactiferous ducts and the two specimens in which moderately severe subepithelial inflammation had occurred, the nipples were microscopically normal. Although microscopic anatomic obstruction of the neck of the ducts was searched for, none was found, except in the aforementioned cases in association with gross deformity.

The epithelium of the ducts near the nipple was normal, but with distention of the duct it thinned and the individual cells tended toward a cuboidal appearance. Occasional vacuolated cells could be found in most specimens. In 6 of the cases there was an increased number of desquamated cells. In 9 additional cases these changes were present and were associated with a great increase in the number of vacuolated cells.

The peripheral ducts usually were lined by smaller cuboidal cells. The number of cell thicknesses was variable and ranged from 6 to 8 down to a single flattened layer or even to complete denudation (Fig. 3, a and b). The largest, most distended ducts or those with the most periductal fibrosis tended to have fewer layers. Those with evidence of little periductal inflammation and minimal dilatation would often have normal epithelium, while those with moderate inflammatory changes and distention had more variations in type. In 12 of the cases an increased proliferation was noted within the ducts, with the formation of masses of cells and tiny papillae with or without anastomosing branches. Some of the small ductules were occluded by this overgrowth but none of the epithelium could be called "atypical." In isolated areas of the ductal wall of 9 of the specimens were found colostrum-like cells which were large, pale and round, with slightly acidophilic cytoplasm and small dense nuclei. The epithelial layer was thickened by masses of these cells which encroached on, or filled, the lumen (Fig. 4, a and b).

A few of the breasts showed no evidence of periductal reaction to the retained secretion, but the great majority had responded with inflammatory changes which ranged from a slight amount of small round cell infiltration to acute abscess formation. The predominant and universally present type of cell was the lymphocyte. Large wandering cells and plasma cells could usually be identified. In some, chronic granulation tissue with proliferating endothelial cells and fibroblasts was seen. Subacute inflammatory changes which were found in 8 of the breasts were characterized by the presence of many plasma cells, an occasional giant cell and a few polymorphonuclear leucocytes (Fig. 5). Acute or subacute abscesses were identified microscopically in 5 of the cases. In 3, there were pseudotubercles, with giant cells and epithelioid cells. In 10 of the breasts a site of rupture of a duct was visualized; invasion of the lumen by granulation tissue and

Fig. 1. Diffuse comedomastitis. The most marked changes are beneath the nipple.

exudate was apparent. Marked chronic inflammatory tissue surrounded these areas and was spread through the stroma. Fat-laden phagocytes were present in the periductal tissues and in the lumen. The finding of hemosiderin-laden histiocytes in the periductal tissues of 8 specimens suggested previous hemorrhage. Periductal fibrosis was often marked so that the ducts were surrounded by concentric rings of hyalin-appearing connective tissue. In these instances the epithelial lining was atrophic and the periductal lymphocytic infiltration was mild to moderate; the infiltrated tissue was separated from the lumen by wide bands of connective tissue.

Fig. 2. Cross section of a nipple. Note great dilatation of the ducts immediately beneath nipple. ×5.

The stromal fibrosis was more evident in the small atrophic glands where it often caused squeezing and distortion of the remaining lobules of the breast. In others, much of the stroma had been infiltrated with fat. In those breasts with evidence of moderate to severe inflammation, the infiltrate extended into the stroma and, in a few instances, the areolar and fibrous tissue of the entire organ was involved.

Usually in the lobules there was only insignificant round cell infiltration. Sometimes, however, the lobules were trapped in the inflammatory exudate which had spread from a nearby duct so that the tubules and acini appeared as scattered epithelial islands in a sea of lymphocytes, with the lobular structure being unrecognizable. Nineteen of the specimens contained scattered, small lobules with fibrosis and a decrease in the epithelial elements. In one or two of these specimens the lobules approached normal, but in most they were definitely atrophic. Early or mild proliferative changes, affecting both the epithe-

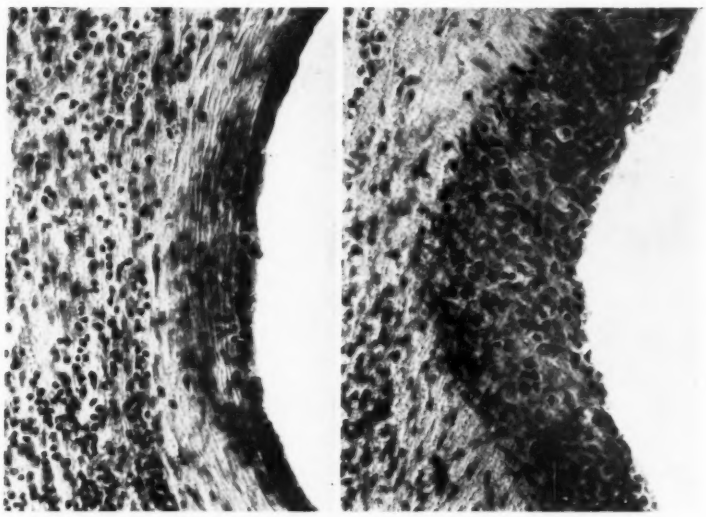
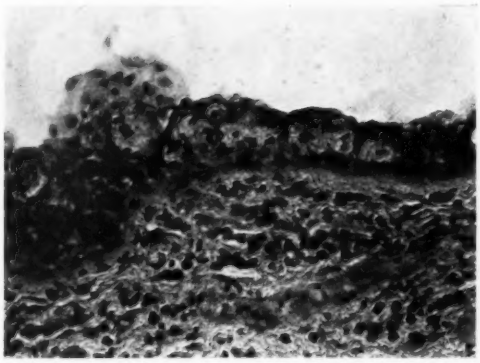


Fig. 3. a, left, The thinning and flattening of the epithelium that frequently accompanies dilatation of the ducts. Note also the subjacent connective tissue and periductal inflammation. ×200. b, Note the thickening that may occur.

lium and connective tissue in the lobules, were present in 35 of the breasts. Sometimes, proliferation of the epithelial cells predominated to give extensive formation of new tubules and acinus-like structures. Occasionally, the stroma was the more active of the two elements, and the scattered, compressed and irregular ductules or acini simulated infiltrating malignant tissue. The tubules sometimes showed small degrees of dilatation that did not correspond with the extent of ectasia in the larger ducts. These changes have been called "adenofibrosis" (54), "mastodynia" (38), "blunt-duct adenosis" (26), "sclerosing adenosis" (26), and "mazoplasia" (14). Not included were those specimens with pale-staining epithelium, but otherwise these changes were similar to those in "fibroadenomatosis microcystica" (48).

In 44 breasts, simple cysts with a lining of cuboidal or flattened epithelium were present. In 43, the cysts were associated with large, pale-staining columnar epithelial cells of the apocrine type, giving the picture of Schimmelbusch's disease. For the most part, the cysts did not share in the inflammatory process that so often accompanied comedomastitis. Occasionally, there was fibrosis of the wall and a moderate amount of reaction, and, at times, the inflammation had spread from the periductal tissues to include a cyst. Apocrine type of epithelium was also found in 22 of the breasts that did not contain macroscopic cysts. Such epithelium was not found in the ectatic ducts and, hence, was not considered as evidence of ductal hyperplasia even though papillae with anastomosing and interlacing branches were found within a cyst. The breasts in which cystic and apocrine changes occurred were referred to simply as those with cysts, those with cysts and apocrine epithelium, or those with apocrine epithelium but without cysts. These would include the cystic disease and adenosis of Geschickter, diffuse papillary cystadenoma of Schimmelbusch, diffuse nonencapsulated cystic adenomatosis of Bloodgood, fibroadenomatosis cystica of Semb and the cystipherous desquamative epithelial hyperplasia of Cheatle and Cutler. The concurring fibroadenoma and fibrosarcoma were typical in appearance and there was no evidence of dilatation of the ducts within them.

During the course of the study, it became evident that most of the diseased breasts fell



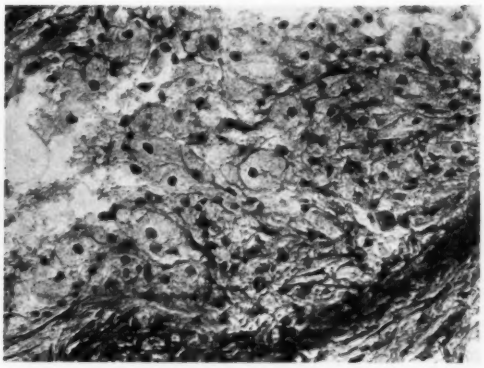
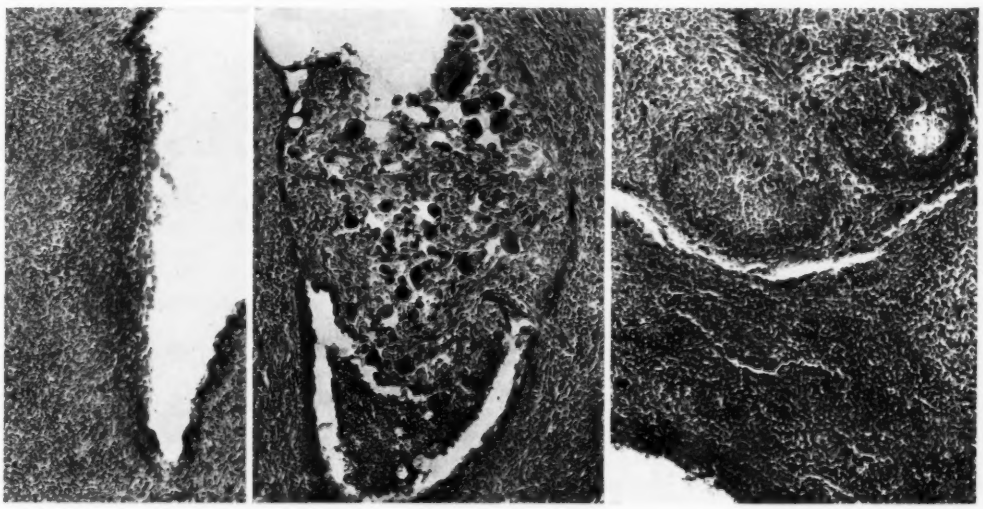


Fig. 4. a, left, Colostrum-like cells found in an isolated area of the ductal epithelium. ×190. b, Heaping up of the colostrum-like cells so that the lumen of the duct is almost occluded. ×190.

into rather well defined groups, based entirely on the pathologic changes observed. Both the gross and the microscopic findings were evaluated in determining the correct place for each. The distribution of the lesions allowed for division of the lot into three groups. The designation "focal" was used when the disease was in one localized part or in scattered parts; "diffuse" indicated involvement of the greater share of the duct system. Since the entire breast had not been removed in 19 instances, the extent of the disease could not be determined and these were called "sectional." The severity of the disease in the ducts formed the basis for subdividing each of these 3 groups into "early" and "advanced." The terms did not refer to the actual time the breast had been involved but indicated the degree of the changes in the breast. In "early" disease, the periductal fibrosis was absent or minimal, the



a b c

Fig. 5. a, Subacute inflammation about a duct with erosion of the lining epithelium. ×66. b, Rupture of the duct and invasion by granulation tissue in which there are many foreign body giant cells. ×66. c, In this section is shown the granulomatous reaction with the formation of pseudotubercles. ×97.

periductal inflammation was minimal to mild, the amount of retained secretion was small and the dilatation of the ducts was minimal to mild (Fig. 6, a). In "advanced" disease the periductal fibrosis was moderate to marked, the periductal inflammation was moderate to marked, there was a large amount of retained secretion and the dilatation of the ducts was moderate to marked (Fig. 6, b and c).

Of the 19 biopsy specimens, 11 showed early stages of the disease and 8 showed advanced. Forty-three of the whole breasts were classed "focal, early." These contained one or more areas of comedomastitis in which the changes in the ducts were slight. Only one could be called "focal, advanced," and it exhibited moderately severe ductal and periductal changes in scattered areas. The "diffuse, early" group consisted of 55 breasts in which there was involvement of most of the ductal system but the changes present were minimal to mild. Forty-five breasts made up the "diffuse, advanced" group, this group included those with the most widespread and most marked disease.

The majority of those specimens with focal or early comedomastitis or both exhibited cystic changes or apocrine epithelium, while the majority of those with marked evidence of diffuse, advanced disease, exhibited atrophic changes or early proliferation. Conversely, in the great majority of those specimens with atrophy or early proliferation, there were advanced forms of comedomastitis, while in the majority of those with cysts or apocrine epithelium or both, early forms of comedomastitis were present.

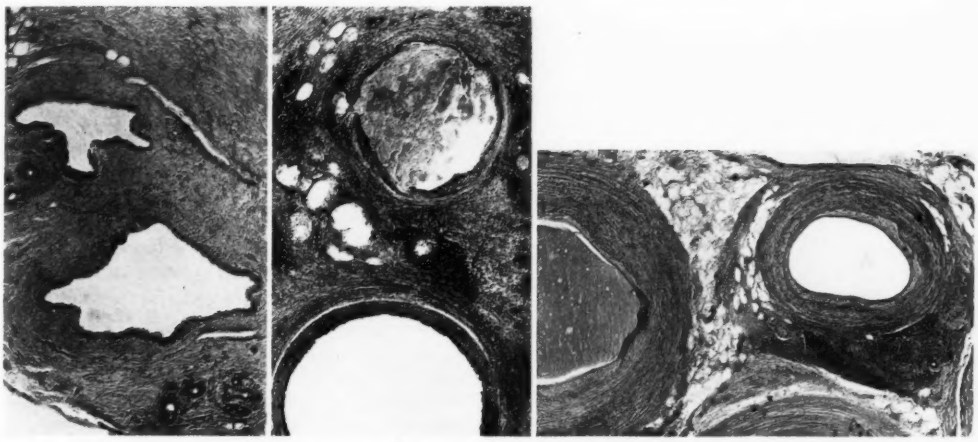
The relationship of the unusual pathologic findings to the type of comedomastitis present is of interest. As would be expected, the "diffuse, advanced" group contained the greatest share of those breasts in which complications had occurred. These complications included rupture of the ducts, deposition of hemosiderin about the ducts, subacute inflammation, abscess formation, presence of pseudotubercles and plasma cell mastitis. In contrast, the findings indicative of secretory activity, which were excess desquamation or vacuolation beneath the nipple and the presence of colostrum-like cells, were confined, with two exceptions, to the "early" group. Surprisingly enough, the percentage of specimens in the "focal" groups which showed secretory activity was higher than that in the "diffuse" groups. The incidence of hyperplasia within the ducts did not vary with the stage of the disease. Hyperplasia was not found in any breast in which atrophic or early proliferative changes were present in the lobules.

CLINICAL FEATURES

Bilateral involvement of the breasts, whether associated with comedomastitis or some other disease, was common. Although a total of 163 benign breasts were examined, there were but 136 patients. Each breast was considered as a separate pathologic entity and such viewpoint has been continued in the presentation of the clinical features. Twenty-seven of the women underwent simultaneous or consecutive bilateral amputations for comedomastitis. Thirteen had clinical mastitis in the opposite breast at the time of examination and 6 of the 13 had undergone excision of a portion of that breast. Nine patients had undergone mastectomy for some type of benign lesion, 2 had undergone mastectomy for papilloma, 10 had undergone radical mastectomy for cancer, and 1 had undergone "mastectomy" elsewhere by means of application of a "paste" for supposed malignancy. Three others had had comedomastitis associated with cancer in the opposite breast. Sixty-five had had a clinically normal breast on the side opposite to that of the operation.

Patients in the focal, early group had had more trouble with other forms of disease of the breast than had those in the other groups, even though fewer of them had bilateral comedomastitis, while in contrast, patients in the diffuse, advanced group more frequently had had bilateral comedomastitis and less frequently had suffered from other forms of disease of the breast. The absence of previous cancer in this latter group may be significant.

All of the patients in this series were white women. Their ages ranged from 28 to 75 years at the time the breasts were removed, with an average age of 45 years. The ages by groups were as follows: sectional, early, 43.3 years; sectional, advanced, 43.3 years; focal, early,



a b c

Fig. 6. a, Early comedomastitis with mild periductal reaction although the ducts are considerably dilated. Note also the increase in fibrosis of the stroma. ×27. b, Advanced comedomastitis with marked ductal distention, periductal inflammation and periductal fibrosis. This specimen also shows the typical appearance of the retained secretion. ×27. c, In this specimen of advanced comedomastitis is clearly demonstrated the heavy rings of connective tissue that sometimes form about the dilated ducts. ×18.

47.9 years; focal, advanced, 53 years; diffuse, early, 44.5 years, and diffuse, advanced, 43.6 years. These figures do not permit the assumption that the disease progresses in degree and severity with increasing age. Fifty-three of the breasts were from postmenopausal women, while 30 were from women who gave a history of menstrual irregularities which were usually associated with the menopause. These irregularities were especially frequent in those with focal, early disease. Thirty-three of the breasts had never been subjected to the stimulus of pregnancy and lactation. Only 4 nulliparas had advanced disease. This was in contrast to the high incidence of milder forms of disease in nulliparas and indicates that the "stimulative" changes associated with pregnancy and lactation may predispose to the development of advanced comedomastitis. Although there was a higher incidence of familial cancer in patients with the early stages of the disease, no significance was attached to this finding.

Symptoms. An attempt was made to determine the principal symptom and its duration. If one judges the onset and duration of the disease from the time of onset of the principal symptom, one finds that those patients with the diffuse, advanced disease had a shorter clinical course than those with other forms. It may be that comedomastitis in itself is relatively silent until the inflammation becomes severe enough to draw attention, while those breasts with cysts are likely to have lumps or pain which draw attention before the less noticeable comedomastitis has developed fully.

A lump in the breast was described in a higher proportion of those patients with advanced disease than in those with early disease. The term "discomfort" was used to include any unpleasant or painful sensation from itching to excruciating pain whether constant, intermittent or cyclic. Because of this interpretation, this symptom was the most common and it was present in a great majority of patients. The occurrence of discharge in 33.3 per cent of those in the diffuse, advanced group appears significantly larger than that of 21.8 per cent for the diffuse, early and 27.9 per cent for the focal, early groups. When a purulent type of discharge was present it was described as gray, green, orange, or brown. More than half of those patients with a history of abnormality of the nipple had marked comedomastitis. Of those with diffuse, advanced disease 26.7 per cent had noticed a

change in the nipple. Of the 6 with congenital inversion of the nipple, 4 had severe disease throughout. The majority of nipple changes were in those breasts in which there were atrophic or early proliferative changes.

No particular emphasis was placed on a history of injury to the breast although 6 of the women did give this information. Not one of the patients directly related her difficulty to the trauma. No determination of the number of lactations or of the duration of each could be made from the case records. Abnormalities of lactation were noted in 10.4 per cent of the breasts, and in more than half of these breasts advanced disease was noted. Of those with prolongation of secretion, the discharge remained milky in one but became purulent in the others. Frequent episodes of nonpuerperal mastitis could be expected in this disease, and the incidence was 14.1 per cent. It was the most common in those patients with the diffuse, advanced disease, although the difference was not as great as might be anticipated.

Signs. The term "nodularity" was used to apply to those breasts described as "granular" or "shotty" or as giving evidence of mastitis or thickening. The breasts so designated made up the largest single group, being especially frequent in association with diffuse, early comedomastitis. The diffuse, advanced group exhibited a great tendency to have a single mass and every breast of this class had some palpable physical finding. In only 2 cases were palpable ducts described as such. There was but little difference in the total number of cases, type of discharge or distribution as to groups previously defined between the cases in which a discharge was expressed from the nipple at the time of examination and those in which a discharge had been noted by the patient. More nipple abnormalities were found by the medical examiner than had been complained of by the patient, but the same trends as to distribution in the three groups were present. More than half of the deformities occurred in association with diffuse, advanced stages of disease. Conversely, in 37.8 per cent of patients with diffuse, advanced disease lesions of the nipple were present.

Induration, edema, redness, or heat were the signs of inflammation, although the occurrence of induration alone was not considered sufficient evidence. These findings could be expected with marked comedomastitis and in more than half of the instances they were associated with severe disease. Whenever fixation of a mass to the skin or nipple is determined on examination, malignancy must be considered, and the occurrence of such fixation in 22.7 per cent of the entire series was remarkable. The rate was even higher (33.3 per cent) when diffuse, advanced comedomastitis alone was considered. No detailed endocrine studies were carried out. In 14 cases some hormonal imbalance was indicated when routine examinations disclosed diabetes mellitus, hypogonadism, hirsutism, myxedema, low basal metabolism without myxedema and hyperthyroidism. Sixty-four of the breasts were from women exhibiting some type of pelvic abnormality.

Those breasts in which some kind of complication developed caused few symptoms or signs that were at variance with those to be expected from the groups to which they belonged. In 3 out of 4 cases of severe comedomastitis with congenital inversion of the nipple multiple complications occurred. In those cases in which there was periductal hemosiderosis, no increase in frequency of bloody discharge occurred. In only 2 of the 5 cases in which microscopic abscesses occurred were clinical signs of inflammation present. Only 3 of those breasts that showed changes suggestive of secretory activity had spontaneous discharge from the nipple, and another had a serous secretion on examination. These changes were not necessarily residua of lactation, as the colostrum-like cells appeared in the breast of one nulliparous single woman. The 2 breasts with subepithelial inflammation were from women with sore nipples.

Diagnosis and treatment. Often the diagnosis of a breast lesion on clinical grounds is expressed in a broad inclusive term, and a specific diagnosis must await the pathologist's examination of tissue. The diagnosis of comedomastitis was made preoperatively but twenty-one times, although the condition was probably recognized more often, and it was included in 64 other cases under the term "mastitis." That comedomastitis may simulate malignancy was only partly illustrated by the

13 cases in which a diagnosis of carcinoma had been made. Many of those called "tumors" (24 cases) and "Paget's disease" (2 cases) were considered "suspicious."

All of the breasts were removed surgically. In 19 of the cases simple excision was considered sufficient to eradicate the involved parts or to prove benignancy. The great majority of the operations consisted of simple mastectomy, but in 2 cases the lesion imitated carcinoma so closely that radical mastectomy was performed.

COMMENT

Retention of secretion, dilatation of the ductal system and periductal mastitis have been shown to be the principal pathologic characteristics of comedomastitis. It appears that the process starts with stasis of the ductal contents with resultant distention. As the more liquid part of the secretion is absorbed the contents become concentrated and viscid. With decomposition or infection, irritative substances are produced and inflammation of the ductal walls and periductal tissues results. Complications may develop that lead to abscess formation or to the extensive subacute inflammation of plasma cell mastitis. A subsidence of the more acute phases is followed by fibrosis and hyalinization of the periductal connective tissues so that the irritant medium is effectively walled off from sensitive tissues. A breast with relatively mild changes could be fairly rapidly changed into one showing marked disease by the introduction of infection or by the erosion and rupture of a duct so as to allow the escape of highly irritant secretion into the areolar tissue. One would expect that the ducts which are the site of extensive periductal mastitis would progress to the stage of fibrosis and hyalinization, but in some instances inflammation is resolved with few traces remaining and the breasts return to a stage that is represented by that of the diffuse, early group. If, for some reason, the factor that produces dilatation of the ducts ceases to operate and drainage of the system takes place, a diffuse ectasia might be wholly or partially relieved, so that the breast would fit the criteria for the focal, early classification, or the tissues might even return to normal. There is no reason to believe that some of the breasts considered in the present study had not been through this cycle in whole or in part. Some of those in the focal, early category which were associated with a history of purulent discharge, nonpuerperal mastitis, or abscess may have had a severe inflammation that left little trace. However, in those with the pathologic changes of severe chronic inflammation resolution could hardly be expected to occur.

The sequence of events as just described seems logical and all stages can be seen. To determine the cause of the stasis is more difficult. It may result from obstruction of the ductal system and retention of normal secretion from increased formation of secretion in excess of the amount that the normal mechanism can eliminate or from a combination of the two. Endocrine imbalance and abnormalities of development may account for the process.

In the cases of comedomastitis in this study there was evidence of obstruction of the mammary ducts. In 6 cases congenital inversion seemed sufficient to impair drainage. These women were unable to nurse and pregnancy increased the chance of trouble. Apparently, the remaining 22 patients with inversion or retraction had acquired deformities which were a result of the inflammatory process within or around the ducts, rather than the cause, although such deformity once acquired would tend to interfere with drainage and increase the stasis already present. The one breast with absence of the nipple was diseased before ablation was done. Inflammation beneath the nipple could cause stasis, but, once again, the stasis is more likely to be an effect. The incidence of some type of abnormality of the nipple in diffuse, advanced comedomastitis was 37.8 per cent and it may be that the majority of the lesions were made worse by the deformity even though the deformity was not the primary cause.

The scarring subsequent to trauma could impede outflow, but no definite connection could be shown in the present study. Inflammatory tissue may occlude the lumina or produce scarring in the stroma of sufficient degree to cause obstruction. Of the 23 instances of nonpuerperal mastitis, only 3 definitely pre-

ceded the comedomastitis, while the remaining 20 were more likely a result of the disease and were to be expected in the natural course of comedomastitis. The 3 breasts associated with a history of lactation abscess and the 5 in which a tender lump had developed in association with lactation may have been the sites of inflammatory or sclerotic changes sufficient to block the ductal system.

While the ducts near the nipple would be the logical site for obstruction, a similar effect might be obtained by blockage of many smaller ducts distally. Such blockage might account for some of the scattered focal lesions and might even be responsible for a few lesions of the diffuse types. Expanding lesions of the breast, especially cysts, and also fibroadenoma and fibrosarcoma could block adjacent and distally located ducts by compression. Intraductal tumors will frequently produce dilatation of the duct distally with retention of secretion and periductal mastitis, but the instances of hyperplasia found in this series were mild and seemed insufficient to be causal.

Theoretically, extramammary pressure from improperly fitted or improperly worn garments could obstruct the normal outflow of the ducts. Large pendulous breasts drag and may distort the ductal system. We have no evidence that either of these was a factor.

Excessive secretion or desquamation will overburden the normal capacity of the ductal system to discharge its contents. Both occur during and immediately after lactation, and lactation does, apparently, have some influence on the development of comedomastitis. Few nullipara have severe disease. The poor drainage associated with inverted nipples has already been considered. The 5 patients in whom a tender lump developed in the breast either during lactation or immediately after its cessation may have had inflammation, overproduction of secretion or both. In 4 breasts a prolongation of the secretory activity occurred after nursing had ended.

The presence of colostrum-like cells in the peripheral ducts and vacuolated or desquamating epithelium or both behind the nipple was probably indicative of secretory activity, although further studies and special staining would be necessary to prove this. Similar findings have been described in association with chronic cystic mastitis and with a disease similar to comedomastitis (14, 27, 33, 52). In the present study the secretory action, if any, did not seem to increase the stasis as stasis occurred more frequently in the mild forms of the disease. The inflammation associated with development of severe ductal lesions could obscure or destroy the evidences of secretory activity but these evidences seemed more closely associated with cystic disease or apocrine epithelium.

There were evidences of cellular activity in response to irritation in almost all of the specimens examined, as most of them showed areas of thickening of the epithelium and some increase in shedding. In the 12 breasts that showed excessive hyperplasia there was an increased amount of desquamation. Infection such as a chronic lactation mastitis might have initiated the triad of stasis, dilatation, and periductal inflammation by distention of the duct with exudate as well as by obstruction of the normal outflow. However, when the inflammatory exudate was a response to the irritants of decomposing secretion, it could not be considered as the primary cause, although the invasion of the lumen of the duct would have augmented the severity of the disease already present.

Atrophic changes in the breast resulting in ectasia of the ducts and retention of secretion are an etiologic factor in older women. Some authors (9, 27) have said that these degenerative changes are primarily responsible for a disease similar to comedomastitis, but others (26, 37, 54) have found this disease in the breasts of younger women which have not undergone atrophic changes and which have presented a variable pathologic picture as was observed in the present study.

The excellent work that has been done on the hormonal influences in diseases of the breast indicates that endocrine glands may control the development of any type of lesions in the breast. In this series there was inadequate evidence of endocrine dysfunction, but the occurrence of comedomastitis at the time of life when endocrine disorders are common may be an indication that it is secondary to some type of abnormal hormonal stimulation. The dila-

tation of the ductal system that is produced in animals by the administration of estrin is similar to that which occurs in the early stages of comedomastitis.

RELATIONSHIP OF COMEDOMASTITIS TO OTHER DISEASES

Chronic cystic mastitis. Comedomastitis frequently is inseparably bound to chronic cystic mastitis; in the present study 144 of the 163 breasts contained macroscopic cysts, apocrine epithelium, or early proliferative changes in the lobules. Often the diagnosis of chronic cystic comedomastitis was made to express the true situation. Indeed, in many of the focal. early cases the comedomastitis was overshadowed by the cystic and apocrine changes. The presence of cystic disease in the breast may explain why there is a lower average age and a shorter clinical course in cases of advanced comedomastitis than in cases of early comedomastitis when one might expect, from the pathologic picture, the reverse to be true. Chronic cystic mastitis may also account for the presence of masses, discharge from the nipple, retraction or inflammation in the breast which is the site of mild, scattered comedomastitis. A truer picture of what can be expected clinically from comedomastitis might be obtained from a study of the diffuse, advanced group alone.

The intimate relationship of comedomastitis and chronic cystic mastitis may be explained on the basis of etiology. The stasis of secretion in the ductal system may be the inciting factor in production of either. Many authors have observed dilatation of the ductal system in cystic disease, and the cysts themselves are usually considered as enlargements of the smaller tubules or acini while comedomastitis involves the larger ones. Why one breast produces cysts and another dilated ducts is not known, although the influence of senile involution, nipple abnormality, intraductal infection or residual postlactation ductal enlargement or inflammation would tend to give comedomastitis. The localized changes of the disease can be secondary to the production of cysts which compress adjacent ducts. Time may prove that the two types are responses to different hormones.

Mammary carcinoma. The etiologic significance of stasis of secretion within the ductal system in the production of neoplasm within the breast has been stressed (2–4, 14, 18, 25, 30, 34, 57). It was stated that the breakdown products of this material were irritant and that they led to epithelial proliferation. The work (56) showing that oleic acid can serve as an activator for mild carcinogens is suggestive. Analysis of retained secretion by Lepper and Weaver showed it to be principally fat with some breakdown products of protein, while Adair and Bagg found lactic and butyric acids in thick creamy discharges from the nipple. Most of these investigators have stated that chronic cystic mastitis is precancerous, and the work carried out in studies on animals corroborates this viewpoint (50).

Others (9, 26, 27, 54) said that there was no relationship between the occurrence of lesions similar to comedomastitis and the development of malignancy. When they described cases of marked retention of secretion, they found no associated cancer even though cancer was found in another portion of the same breast. In most of those breasts in which neoplastic changes occurred, the dilatation of the ducts with retention of secretion was considered incidental to malignant change.

In our series, while we were procuring specimens of comedomastitis, every case in which that diagnosis had been made was included, and it was found that 23 of the breasts contained concurrent papilloma and 18 contained carcinoma. The presence of the tumor was the only differential point in the gross pathologic appearance. Although the comedomastitis was less advanced and the incidence of hyperplasia was much higher when neoplasia was associated, the changes in the ductal system were of the same order as in the benign series. Breasts which contained cysts or apocrine epithelium or both formed the large majority of the cancerous group. The possibility that most carcinomas associated with comedomastitis arise from the ductal system as comedocarcinoma was suggested by the finding of comedocarcinoma in 5 cases and comedo areas in 5 of the infiltrating growths.

The tendency to bilateral disease of the breast was present although it was less definite

in the cases in which papilloma was present. One patient had bilateral comedomastitis and papilloma and another had bilateral comedomastitis and carcinoma. In 3 patients, the remaining breast was removed for benign comedomastitis subsequent to a radical operation for comedomastitis and cancer of the opposite breast. All of the patients with bilateral disease of the breast had cysts or apocrine epithelium or both. Although the youngest patient, aged 16 years, was in the group with papilloma, the average age in these cases of malignant disease was slightly higher than that in the benign series; however, the difference was not as great as one might have expected if the comedomastitis had been primary and the neoplasia had supervened. The duration of the clinical disease indicated that the disease in those patients with neoplasms had a slightly longer time in which to develop; however, this determination was made from the time of onset of the principal symptom, which was usually associated with the tumor. The incidence of nulliparity is much higher in cases of comedomastitis associated with papilloma than it is in cases of comedomastitis associated with carcinoma; in turn, the incidence of nulliparity in cases of comedomastitis associated with carcinoma is slightly higher than it is in cases of benign comedomastitis. There was more familial carcinoma in those patients with neoplasia. The clinical features were predominantly those of the presence of the tumor mass; little evidence of the comedomastitis was present. There was nothing to indicate that the comedomastitis antedated the neoplasia. Indeed, the reverse may have been true because neoplastic changes may have caused obstruction of the ducts and an increase in desquamation.

In comedomastitis, retention of secretion occurred in the most extensive degree, and while the stages of the disease were not definitely fixed, they were a good indication of the degree of stasis and of the amount of irritation and inflammation that occurred. Instead of the most advanced forms of the disease being found in association with neoplastic changes, the reverse was true. The irritant quality of the secretion was obvious from the amount of inflammatory infiltrate and the epithelial thickening that occurred, to some extent, in all but the cases of earliest comedomastitis, but hyperplasia sufficient to give cell massing and branching forms was infrequent in the benign cases and occurred then only in those breasts that presented other evidence of a growth stimulus in the form of cystic changes or apocrine epithelium. The hyperplasia that was found in association with neoplasia was much more exuberant and much more common than that which was not associated with neoplasia. There was no correlation between the stage of the comedomastitis and the extent or incidence of this overgrowth. There were fewer breasts with atrophic or early proliferative changes in the carcinoma series than in the series with nonmalignant lesions.

No additional cases of early carcinoma arising in comedomastitis were found. Two cases that were originally considered carcinoma could not be verified as such in our section. None of the malignant areas could be traced directly to origin in a focus of comedomastitis. Indeed, there was no indication that progression or prolongation of comedomastitis led to an increase in hyperplasia or neoplasia or both. It may be that the ductal lining is resistant to the proliferative stimulus as Geschickter suggested. Apparently neoplasia, when it occurs along with comedomastitis, has a different inciting agent from that of comedomastitis.

Plasma cell mastitis. Ewing (24) commented on plasma cell mastitis that "the main gross anatomic feature is the presence of many such thickened ducts, which are filled with puriform material, and may extend over a large segment or the whole of the breast." In other descriptions (1, 19, 20, 39, 41, 45) the presence of large ducts with retained secretion has also been given as an important feature of this disease. Others (27, 33, 57) have stated that there is a close relationship between plasma cell mastitis and comedomastitis or a disease similar to comedomastitis.

Examples can be found that show every stage in the development of plasma cell mastitis from comedomastitis. In some of the cases of comedomastitis subacute or chronic inflammation about the ducts, presumably due to the leakage of ductal content into sensitive periductal tissues, may be evident. In these

cases may be found giant cells, foam cells, and plasma cells. One patient with bilateral breast disease illustrated the transition very well. In the breast on one side there was typical cell mastitis, while in the opposite breast there was comedomastitis which varied from mildness in some areas to severity in other areas as evidenced by the presence of granulation tissue which contained plasma cells, foam cells and foreign body giant cells. In other breasts of the series subacute inflammation and even pseudotubercles were present, but these lesions were considered those of comedomastitis.

It cannot be stated from this study that plasma cell mastitis is invariably the result of comedomastitis, but it does seem to be a stage in the same disease process.

Traumatic fat necrosis. Traumatic fat necrosis as described by Lee and Adair may be related to, or identical with some forms of comedomastitis. There is similarity in appearance. Foote and Stewart expressed a belief that some changes associated with stasis and periductal mastitis fit the picture of traumatic fat necrosis. Cole stated that fat necrosis may be identical with plasma cell mastitis if there is minimal liquefaction of fat. Rodman and Ingleby stated that plasma cell mastitis, infected galactocele, traumatic fat necrosis and lactation mastitis are all parts of the same process.

Fibroadenoma. There was no indication that fibroadenoma had direct connection with any of the cases of comedomastitis aside from the action of any tumor in obstructing adjacent ducts. One case has been reported (37) in which fibroadenoma associated with dilated ducts was found in a breast similarly affected.

Other diseases. Cases described as chronic galactorrhea, chronic lactation mastitis and so forth may be variations of cases of comedomastitis in some instances, but they do not appear to be identical.

CONCLUSIONS

1. Comedomastitis is a disease characterized by stasis of secretion, dilatation of the ducts, and periductal mastitis.

2. The clinical features of the disease vary widely, but the disease may be suspected in the presence of a history of abnormality of lactation, nonpuerperal mastitis, discharge from the nipple or abnormality of the nipple. On examination the lesion may closely simulate carcinoma because of the indurated, fixed mass and retracted nipples.

3. Comedomastitis usually is associated with chronic cystic mastitis which may overshadow it clinically.

4. Neoplasia, although it occasionally occurs in the same breast as does comedomastitis, is probably not related to the latter etiologically. By simple obstruction of the mammary ducts such neoplastic changes may, at times, produce a focal comedomastitis.

5. Plasma cell mastitis is probably a form of comedomastitis.

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RESULTS OF TREATMENT OF CARCINOMA OF THE OVARY WITH DATA ON THE AGE INCIDENCE OF THIS DISEASE

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A REVIEW of the literature on malignant epithelial tumors of the ovary leaves some doubt as to the value of roentgen therapy in this disease. Most of the previously reported series of cases show little if any benefit as a result of such therapy. Most authors have recommended that x-ray treatments be given as a palliative measure in the more advanced cases. They have admitted that the dosage given to many of the patients was less than optimum as judged by present standards.

It is unfortunate that in the majority of cases the disease is of an insidious nature and that in most hospitals the operability rate is less than 40 per cent. It is also unfortunate that even for those patients judged operable at the time of exploration the cure rate is distressingly low. It appears obvious, therefore, that the proper treatment for carcinoma of the ovary has not yet been found.

Walter, Bachman, and Harris in 1941 reviewed the literature up to that time and reported a series of cases from Mount Sinai Hospital in New York. Of 63 cases of all stages of the disease in which surgery was the only form of treatment, 24 per cent were alive at the end of 1 year and only 6.3 per cent at the end of 5 years. Of 31 patients treated by means of surgery followed by adequate roentgen therapy 87 per cent were alive at 1 year and 29 per cent at 5 years. At first glance one may be inclined to discount their figures, since the group receiving roentgen therapy contained a smaller number of advanced cases than did the group having surgery alone. However, their figures may be further subdivided to show that for the cases judged operable and having surgery only, the 5 year salvage rate was 21 per cent; whereas, the operable group in which patients had surgery plus roentgen therapy showed a salvage rate of 40 per cent. Of the advanced cases in which patients had surgery alone none was alive at 5 years, whereas similar cases in which patients received postoperative x-ray treatment showed 18 per cent survivals at 5 years. It thus appears that the chance for survival was definitely increased when postoperative x-ray treatments were given.

The same authors believed that histological grading played a minor role in prognosis, and that the extent of the disease was of much greater importance. They concluded that x-ray therapy was of real value in the treatment of ovarian cancer, and that the surgeon should not take too great risks in an attempt to remove the last fragments of diseased tissue, but should instead rely on postoperative roentgen therapy.

Other authors (3, 4, 8, 9) have reported series of 100 or more cases with 5 year survival rates which vary from about 15 to 35 per cent. Within these groups of cases there has undoubtedly been some variation in the type of material seen, in the interpretation of the histology, and in the vigor with which postoperative radiation was given. The highest survival rate appears to be that of Lynch who reported 35.5 per cent in a group of 62 proved cases alive and well at 5 years. He refers to 2 cases in which operation was known to be incomplete, but the patients lived 13 and 17 years following x-ray therapy. He also reports one proved recurrence after 13 years, and calls attention to several cases of long duration in which patients had little or no x-ray therapy but in whom peritoneal implants apparently regressed following removal of the primary tumors. Pemberton in 1940 believed that the operation should be as radical as circumstances would permit and should be followed by x-ray treatment. Taylor and Greeley in 1942 were able to show little or no improvement in their

survival curve by giving postoperative radiation, but believed it probable that in an occasional case x-ray therapy was an essential factor in producing cure.

The group of cases which we wish to report shows a salvage rate which is no higher than that already reported by other authors. We do believe, however, that adequate x-ray therapy may be of very real value to these patients and that it may occasionally be curative. We therefore find ourselves in partial disagreement with Meigs (4, 5, 6) who believes that x-ray therapy "has never cured patients, but it has helped to make them live longer."

We wish to report the series of patients seen in the department of roentgenology of the New England Deaconess Hospital during the 10 year period beginning in June, 1936. The series consists of 76 patients, 57 of whom have now been followed to death. Of the original group, 14 were alive more than 5 years after their first operation and treatment, but 3 of the 14 have since died of their disease, and one is alive at 5½ years with recurrent disease. Not all of the patients have as yet had an opportunity to live 5 years after treatment, but the 5 year survival rate calculated by the method of Nathanson and Welch is 21 per cent.

It comes as no surprise to find that the 2 patients having stage 1 disease are alive and apparently well 7½ and 8 years following treatment. Of much greater interest are those who survived more than 5 years in spite of the fact that when first seen their disease was too extensive to permit complete surgical removal.

Such a patient was first operated upon in another hospital where large masses had been found in both ovaries. Multiple smaller nodules were scattered through the pelvis and in the general peritoneal cavity where there was a large amount of exudate. The fluid had been removed and a biopsy done. Histological examination had shown papillary cystadenocarcinoma. She was then seen by Dr. E. M. Daland who referred her to us for x-ray therapy. She was given 1900 roentgens to each of two anterior and two posterior pelvic ports with 1500 roentgens to each of two upper abdominal ports. Ports measured 15 by 15 centimeters and all treatments were given at 400 kilovolts with other factors as noted below. About 6 weeks later she was again operated upon. On this occasion there was no evidence of disease outside the pelvis and there was no abnormal amount of peritoneal fluid. Ovarian tumors were still present but were smaller than at the time of the first operation, and were removed. Another period of 6 weeks was allowed to pass and she was then given a second series of x-ray treatments. These treatments were given through the six ports first used and with the same factors. The last treatment was given on September 30, 1938. Since that time she has been well except for gradually increasing evidence of radiation damage to the skin and subcutaneous tissues. In May, 1946, it was necessary to excise an area over the sacrum and replace it with a graft. There is still no evidence of recurrent ovarian tumor.

Six other patients in the group of 14 survivors have received equally large amounts of treatment to the pelvis, but in only 2 others has treatment been given to the upper abdomen. Their skin and subcutaneous tissues show varying degrees of atrophy and telangiectasia, but only the one has so far required excision and graft. No patient in the surviving group has had less than 1800 roentgens to each of four pelvis ports.

In each case an effort was made to plan the treatment so that all diseased tissue would be included within the ports. If operation had shown the disease to be confined within the pelvis the treatments were given through two anterior and two posterior pelvic ports. In all except very small women the ports measured 15 centimeters square in order to be sure to include the entire pelvic cavity. In previously untreated patients the ports were usually directed straight through the pelvis. Except in the aforementioned case, a second or third course of treatments was not given unless there was objective evidence of residual or recurrent disease. If such disease became manifest in the form of a discrete mass, the subsequent treatment was usually directed toward it through ports which would crossfire the mass, and when such a mass seemed to be confined to one side of the pelvis it was usually

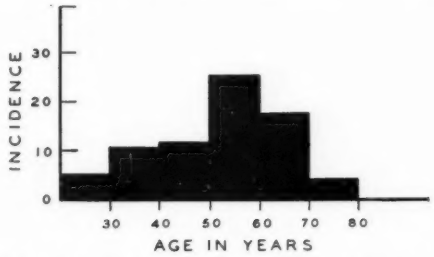

Fig. 1. Series incidence of 74 cases of carcinoma of the ovary.

treated through anterior, posterior, and lateral ports.

If operation had shown the tumor to involve the general peritoneal cavity as well as the pelvis, treatments were planned for four pelvic ports and two upper abdominal ports, provided the general condition of the patient would permit such an extended series. In such cases the four pelvic ports were treated first and the upper abdominal ports were the ones which were slighted if it became necessary to stop the series before the entire plan could be carried out.

When the disease was far advanced and exudate was the chief problem, treatments were usually given through four anterior abdominal ports. Such ports usually measured 15 centimeters square and were frequently tilted slightly toward the midline in order to conform to the contour of the abdomen.

The original plan of treatment almost always called for 1800 roentgens (measured in air) per port whether or not the beams were crossfired, but modifications of the plan were frequently required as the series progressed. Treatments were given at 400 kilovolts with 50 centimeter target to skin distance and with a filter of 0.9 millimeter tin, 0.25 millimeter copper, and 1.0 millimeter aluminum. The normal daily dose was 300 roentgens to a single port, and treatments were given daily except Sundays.

The group of patients in whom long term survival was not secured were frequently benefited in a palliative sense by x-radiation. Illustrative of that group was a woman who had been operated upon elsewhere 7 years previously because of carcinoma of the ovary.

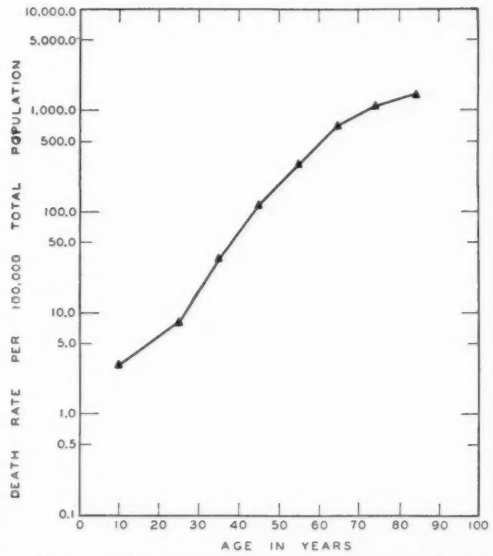

Fig. 2. Death rate for cancer of all types in Massachusetts for 1930. The curve quickly goes off the page unless a semilogarithmic scale is used.

When seen by us there was a hard mass which extended upward to the level of the umbilicus and there was a large amount of peritoneal exudate. Paracentesis had been necessary every 10 to 14 days during the recent past because of the rapid production of the fluid. She was given 1800 roentgens to each of four anterior abdominal ports and did not require paracentesis thereafter. The mass persisted in spite of a second series of treatments which was given 7 months later through four pelvic ports. She died 14 months after her first series of treatments.

AGE INCIDENCE

During the course of study of this group of cases we wished to know whether or not the age of the patients was in any way unusual. Figure 1 was therefore constructed in order to show the number of patients afflicted during each decade of life. At first glance the chart did not appear in any way unusual, and it was obvious that the largest number of patients were in their sixth decade when the diagnosis was made. The number of persons under 30 years of age was approximately the

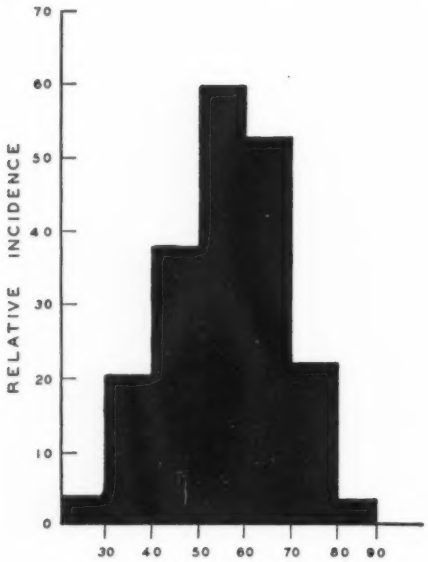

Fig. 3. Age specific incidence of 494 cases of carcinoma of the ovary.

same as the number of those over 70 years old.

The chart was then corrected in order to take into account the number of females living in Massachusetts in each decade of life. The greatest frequency for the disease was again in the sixth decade, and although the incidence over age 70 was then approximately eight times the incidence under age 30 it was still only about one-third the incidence of the sixth decade. The series was admittedly small for any study of age incidence, but the apparent decrease in rate after age 60 was of considerable interest, since the age specific death rate (and incidence) for most types of cancer rises sharply with advancing years. The age specific death rate for cancer of all types in the United States for 1940 was 61 per 100,000 persons living between the ages of 35 and 44 years, 369 per 100,000 between 55 and 64 years, and 1,183 per 100,000 for persons over 75 years of age (2). These rates are almost identical with those computed for Massachusetts for 1930 (1). Organ specific rates have also been computed from Massachusetts data for cancer of the breast, uterus, urinary bladder, skin, and buccal cavity. In each case the rate rises steadily with advancing years, although the rate of rise varies independently for each organ.

We are not aware of previously published data concerning the age specific incidence of carcinoma of the ovary. The records of 420 histologically proved cases have been consulted in addition to those of the 74 proved cases already noted. The age recorded is that at the time when the patient was first seen because of the ovarian cancer. A total of 125 cases are from the Palmer Memorial unit of the New England Deaconess Hospital, 89 from the Peter Bent Brigham Hospital, 154 are from the Massachusetts General Hospital and 126 from the Pondville State Hospital for Cancer. The figures for the Massachusetts General Hospital and the Pondville State Hospital were kindly obtained for us by Drs. J. V. Meigs and Langdon Parsons. Figure 3 shows the incidence by decades for the group.

SUMMARIES OF CASES SURVIVING 5 YEARS

CASE 1. Panhysterectomy was performed in a patient aged 53 years. A tumor which involved primarily the right ovary and extended to a loop of bowel was resected, followed by x-ray treatment consisting of 1800 roentgens through 4 pelvic ports. Patient was well 7 years.

CASE 2. Panhysterectomy was done in a patient of 34 years. Implants were noted throughout the pelvis and abdomen. She was given 1800 roentgens through 4 pelvic and 2 upper abdominal ports. She was well 6 years.

CASE 3. Patient aged 30 years had an exploratory laparotomy elsewhere, 5 months previously. Mass now extends to umbilicus. At second operation tumor was found adherent to both lateral walls of the pelvis. Gross disease known to be left behind where it enveloped ureter. She was given 1800 roentgens through 2 large pelvic ports. Eighteen months later she was given 2000 roentgens through 4 pelvic ports because of a tender mass on left. Eight months later she was given 1500 roentgens through 4 pelvic ports plus 1200 roentgens through a left lateral port. Seven years after first treatment she began to have trouble with a rectal stricture, evidently due to irradiation. Colostomy was done 1 year later. She died 9 years after the first operation.

CASE 4. Patient aged 48 years had had a panhysterectomy elsewhere, in 1926, for presumed benign cystadenomas. In 1937, a mass adherent to the bladder, sigmoid, and pelvic walls was excised. The mass is now histologically malignant. X-ray therapy consisted of 2000 roentgens through 4 pelvic ports. Patient was well 9 years.

CASE 5. Patient aged 45 years had had a panhysterectomy. It was found that a tumor had invaded the uterus and was adherent to the pelvic wall. She was given 2100 roentgens through 4 pelvic ports. Patient was well 6 years.

CASE 6. Patient aged 39 years had been operated upon elsewhere in 1929 for a malignant papillary tumor of the ovary. Roentgen therapy had been given elsewhere in 1932. Patient was first seen at New England Deaconess Hospital in 1939 when she presented a tender mass in right side of pelvis. She was given 1800 roentgens through 4 pelvic ports. Two years later a colostomy was done elsewhere because of obstruction of the colon. There was an extensive tumor in the pelvis but none was seen in the upper abdomen. She was given another course of 1500 roentgens through 4 pelvic ports. She died 15 years after the first operation, 5 years after the first treatment by us.

CASE 7. Patient aged 43 years was operated upon elsewhere 7 years previously for papillary adenocarcinoma. When seen at New England Deaconess Hospital she presented a mass with exudate. Examination of the fluid revealed tumor cells. She was given 1800 roentgens through 4 abdominal ports. No further fluid was found but the mass persisted. Seven months later she was given 1800 roentgens through 4 pelvic ports. She died 7 months later, 8 years after operation.

CASE 8. Patient aged 59 years had had a panhysterectomy. A tumor adherent to the pelvic wall and rectum was found. Roentgen therapy consisted of 1800 roentgens through 4 pelvic ports. She was well 7 years.

CASE 9. Patient aged 53 years was given 1800 roentgens through 4 pelvic ports, following panhysterectomy. She was well 8 years.

CASE 10. Patient aged 34 years had had an exploratory laparotomy but only biopsy specimens were taken. Implants were noted throughout the pelvis. She was given 1800 roentgens through 2 large pelvic ports. Three months later she was given 1800 roentgens through 4 abdominal ports. Five months later she showed persistent mass in the pelvis and was given 1500 roentgens through 4 pelvic ports plus 600 roentgens through 2 lateral ports. One year after first operation panhysterectomy was accomplished in spite of dense adhesions. Histological examination of tissue showed malignant papillary cystadenoma with radiation reaction. Patient was well 7 years after operation.

CASE 11. Patient aged 31 years was given 1800 roentgens through 4 pelvic ports after a left oophorectomy. She was well 8 years.

CASE 12. Patient aged 43 years had had an exploratory laparotomy elsewhere which revealed large masses in each ovary and smaller nodules elsewhere. Abundant fluid was present. Biopsy was done. She was given 1800 roentgens through 4 pelvic ports plus 1500 roentgens through 2 upper abdominal ports. At second operation masses were removed, followed by the administration of 2000 roentgens through 4 pelvic ports plus 1500 roentgens through 2 upper abdominal ports. A radiation ulcer over sacrum was excised 7½ years later. No evidence of residual tumor was found.

CASE 13. Patient aged 60 years had had a panhysterectomy. A mass was adherent to the pelvic wall. She was given 1800 roentgens through 4 pelvic ports. Treatment was repeated 4½ years later because of the presence of a mass in right side of the pelvis. She was alive but with residual disease at 5½ years.

CASE 14. Patient aged 39 years had had a panhysterectomy. Multiple implants were noted in the pelvis. She was given 1800 roentgens through 4 pelvic ports. Treatment was repeated 4 months later. She was well 9 years.

CONCLUSIONS

We believe that x-ray therapy should be employed in *all* cases of carcinoma of the ovary, that it is excellent insurance postoperatively even when the surgeon believes that all disease has been removed, and that it may occasionally result in cure even in advanced stages of the disease.

We believe that the surgeon should not take too great risk in his attempt to remove the last fragments of diseased tissue, but that he should remove the easily accessible masses and then rely on x-ray therapy in adequate dosage and through whatever ports may be necessary to cover the involved areas.

X-ray therapy may bring about gratifying palliation even when cure is not obtained. It often gives relief of pain and causes a retardation of the production of peritoneal and pleural fluids.

The age specific incidence of cancer of the ovary is unlike that of most other types of malignant epithelial tumors since it falls after the sixth decade.

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STREPTOMYCIN IN THE SURGERY OF PULMONARY TUBERCULOSIS

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THE medical sections of the Veterans Administration, the Army, and the Navy have been conducting a cooperative study of the bacteriostatic action of streptomycin on the tubercle bacillus. This study has presented American medicine with a unique opportunity. Never before has such a wealth of clinical material and trained medical personnel been immediately available for research on a new therapeutic agent.

The surgical divisions of the 47 participating study units were asked to determine whether streptomycin provides any protection against postoperative spread or reactivations and against the development of empyema in patients subjected to thoracoplasty and pulmonary resection for tuberculosis.

The program was initiated in January, 1947. After that date, every alternate patient subjected to thoracoplasty and every patient undergoing lobectomy or pneumonectomy was given streptomycin as a protective agent. It was felt that the use of controls in resection cases could not be justified under present conditions. The experience of leading clinics in this country had demonstrated that the mortality and morbidity rate following such procedures was so high as to be almost prohibitive. Six hundred resections for tuberculosis have been reported in the American literature since 1933. Five hundred and twenty of these have been performed since 1942. The total mortality rate in this group was 25 per cent. Empyema followed in 12 per cent of the operations and bronchopleural fistula occurred in 8 per cent. It was considered that these reports offered a sufficient background of experience with which to compare the streptomycin treated patients. If the drug were of value, it would seem mandatory to use it in every patient undergoing resection in an effort to brighten this rather gloomy picture.

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Thoracoplasty, on the other hand, has become standardized by several generations of thoracic surgeons and in recent years has been accompanied by few complications. The number of spreads or reactivations reported in series from the larger thoracic surgical centers has varied between 3 and 6 per cent with empyema a rare complication. The use of controls was considered essential to the study.

In the beginning, 2.0 grams of streptomycin per day were given by intramuscular injection, divided into 5 doses. On October 15, 1947, the standard daily dose was reduced to 1.0 gram, divided into 2 doses of 0.5 gram each at 12 hour intervals. This reduction in dosage was made as a result of experience gained in the larger study of pulmonary and extrapulmonary tuberculosis of which this surgical investigation constituted a part. It was desired also to avoid, as far as possible, the development of resistance to the drug. Resistance had been shown to develop rather uniformly after 6 to 8 weeks of treatment. Under both regimens the drug was administered for 1 week before and 2 weeks after each operation. Since the usual interval between thoracoplasty stages was 3 weeks and the number of stages per patient averaged 3, continuous administration of streptomycin for 9 weeks has been the rule in the thoracoplasty series.

The operating surgeons in each of the member groups were designated or approved by the Veterans Administration Central Office. A further condition of the study was that the indications for operation should not vary from those in use at the respective clinics before streptomycin was employed.

An analysis of the individual reports from the contributing groups indicated that thoracoplasty operations had been performed in 28 hospitals. The number of patients operated upon at each hospital varied from 1 to 99. In both the treated and control groups, 1,347 stages of thoracoplasty were performed.

In the group of streptomycin treated patients, 699 operations were performed upon 258 patients. Postoperative spreads or reactivations resulted in 14, the majority of which were actually reactivations of pre-existing disease. Fifty per cent of the 14 occurred after the first stage. Thus spreads followed thoracoplasty in 2 per cent of the operations in patients treated either with 2.0 grams or 1.0 gram of streptomycin daily. In this group there were 8 wound infections, or 1.1 per cent.

In the group of control or untreated patients there were 249 who underwent 648 operations. Among these there were 36 spreads or reactivations reported. Wound infection occurred following 16 operations. Expressed in terms of per cent, spreads occurred in 5.6 per cent and wound infections in 2.4 per cent. In all respects except for the use of streptomycin, these groups were handled in a similar manner.

A reduction in the occurrence of spreads from 5.6 to 2.0 per cent by virtue of streptomycin protection in a consecutive series of 1,347 thoracoplasty stages would seem a logical conclusion to be drawn from this study. If correct, it certainly is of statistical significance. Analysis of the reports from the individual hospitals, however, indicate that, in some of the larger centers, no such discrepancy between the groups of treated and untreated patients occurred. Some of those clinics were able to demonstrate that, in the years prior to the discovery of streptomycin, postoperative spreads had been held to a comparable figure.

There remains, however, a definite impression that streptomycin will make it possible to accept for operation many patients in whom the disease is too widespread or of too unstable a character to permit a thoracoplasty without its protection.

These facts were considered by the entire Conference[1] and a decision was reached to discontinue the streptomycin study insofar as it pertained to thoracoplasties. The consensus was that the reported reduction in spreads was significant but that other factors such as improvement in anesthesia and surgical techniques, and in preoperative and postoperative care, as reported by some member groups, might have influenced the results. It was agreed to permit each surgeon to continue the use of streptomycin in cases which in his judgment were questionable risks but in which the operation was necessary if the disease was to be controlled.

[1]Fifth Veterans Administration Streptomycin Conference, meeting in Chicago, Ill., April 15–18, 1948.

TABLE I.—COMPLICATIONS IN PULMONARY EXCISIONS TREATED WITH STREPTOMYCIN

	No. of patients	Spread	Bronchopleural fistula	Empyema	Wound infection	Deaths	
						Operative	Nonoperative
Lobectomy Treated 2.0 grams	34	2	2	1	0	0	1
Treated 1.0 gram	43	0	3	2	2	1	0
Pneumonectomy Treated 2.0 grams	29	1	2	1	3	2	0
Treated 1.0 gram	23	1	1	1	1	2	0
Total	129	4	8	5	6	5	1

In the pulmonary resection group, the results in patients operated upon with streptomycin protection were so superior to all those previously reported as to leave little room for doubt as to its value.

There were 129 resections performed, 77 lobectomies and 52 pneumonectomies. Sixty-three of these patients were given 2.0 grams of streptomycin daily, divided into 5 doses, 66 were given 1.0 gram daily, divided into 2 doses. The results as shown in Table I indicate that the 1.0 gram is as efficacious as the 2.0 gram dose.

Fifty per cent of the patients have had a postoperative follow-up of from 6 to 14 months. It is far too early to make other than a preliminary estimate of sputum conversion, but the figures reported indicate that concentrated specimens of sputa are negative to date in 73 per cent of these patients. There were postoperative spreads following 4 operations, or in 3.1 per cent. One of these was of questionable character. Bronchopleural fistulas followed 5.7 per cent of the operations and empyema 4.0 per cent. There were 5 operative and 1 nonoperative deaths, a mortality rate of 4.5 per cent.

A reduction of the mortality rate accompanying lobectomy or pneumonectomy for

tuberculosis from 25 per cent, as reported in the immediate pre-streptomycin era, to 4.5 per cent in a large series of streptomycin treated patients is of tremendous significance. The reduction in occurrence of postoperative empyema from 12 per cent to 4 per cent is also dramatic. While other factors pertaining to anesthesia, surgical technique, and postoperative care may have aided in these results, the fact seems unquestionably established that streptomycin has made resection for pulmonary tuberculosis feasible and reasonably safe.

In addition to the thoracoplasty and pulmonary resection groups, there were reported 8 open pneumonolyses, 8 decortications, 10 extrapleural pneumonolyses with lucite ball plombage, and 12 cavernostomy closures, in all of which streptomycin was used as prophylaxis. There were no spreads or other serious complications reported among these patients. The number of operations reported from any one unit was not large enough to be of statistical significance. The favorable results so far reported, however, indicate that the use of streptomycin may be extended to any thoracic surgical operation, for tuberculosis, in which the possibility of spread, empyema, or fistula presents a threat to the success of the surgery.

DISCUSSION

This study seems to indicate that streptomycin has a protective action against spreads following thoracoplasty for tuberculosis. The operation of thoracoplasty, however, had become so standardized and the complications so few in the pre-streptomycin era that this fact is difficult to establish unequivocally. Since the development of resistance to the drug is common after 6 weeks of treatment, it was felt that the degree of protection obtained was not of sufficient value to warrant its routine use. If a resection should be required at a later date, the resistant patient would be at a distinct disadvantage since there is experimental evidence which suggests that treatment in a resistant patient may be injurious. The majority of participating surgeons at the Conference were of the opinion that thoracoplasty can be performed by virtue of streptomycin protection on a few patients who would have been rejected because of the exudative character of their disease if the drug were not available.

There was unanimous agreement that the use of 1.0 gram of streptomycin daily for 1 week before, and for 2 weeks after, resection should be continued without the use of alternate controls. The reduction in mortality rate and in the frequency of occurrence of postoperative spreads, empyemas, and bronchopleural fistulas offers apparently incontrovertible evidence of the protective action of streptomycin in pulmonary resections for tuberculosis.

CONCLUSIONS

1. The results of a co-operative study concerning the protective action of streptomycin in 1,347 thoracoplasty stages and 129 pulmonary resections for tuberculosis are presented.

2. Streptomycin should not be given to the routine thoracoplasty patient but should be reserved for the occasional borderline risk patient in whom the disease is more widespread and more exudative in character than is usually considered suitable for surgery.

3. The use of streptomycin before and after operation in every pulmonary resection for tuberculosis is considered mandatory.

NOTE.—The information contained in the report of "Streptomycin in Surgery of Pulmonary Tuberculosis" represents the combined efforts of a large group. The accumulation of these data could not have been accomplished without the unselfish co-operation of bacteriologists, internists, and surgeons, guided by expert statisticians.

Since Dr. Murphy was actively engaged in this project and had a significant personal series, he was asked to prepare the combined report.

This endeavor may well serve as a model for future combined research projects.

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THE LUMBOSACRAL ARTICULATION

A Roentgenologic and Clinical Study with Special Reference to Narrow Disc and Lower Lumbar Displacement

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SINCE the early investigations of Goldthwait on the anatomy of the lumbosacral articulation in its relationship to low back and sciatic pain, numerous observers have recorded their findings which have emphasized the importance of this anatomic area in patients with these complaints. The studies of Von Lackum revealed the vulnerability of the lumbosacral area to trauma and degenerative change. Danforth and Wilson described the relationship between the lower lumbar nerves, the intervertebral foramina, the lumbosacral facets and the lumbosacral disc in the etiology of sciatic pain. Ayers reported the frequency of narrowed fifth lumbar intervertebral disc in patients presenting the sciatic syndrome. Williams expressed the opinion that the fifth lumbar disc was narrow in the majority of cases of sciatica and frequently in so called lumbago. Badgley, reporting a large series of patients with sciatic pain, noted narrowing of the fifth lumbar disc in 57 per cent. All of these and many other observers felt that the disc narrowing was due to developmental, traumatic, and degenerative changes, and that there was frequently associated displacement of the lumbosacral articular facets, with degenerative changes in the cartilage of the facets and narrowing of the intervertebral foramina. Ferguson, however, denies any relationship between narrow lumbosacral disc and the incidence of sciatic pain. Barr and Mixter state that a narrow lumbosacral interspace occurs about as frequently as other congenital abnormalities and should be considered as an incidental finding unless there is associated sclerosis or spur formation. Willis noted narrow disc in only 7.6 per cent of a series of patients with back and leg pain. Some writers described congenital narrowing of the disc while others attributed such observations to the presence of transitional vertebrae, the immature disc being mistaken for the true lumbosacral disc. Posterior protrusion of the disc, noted very early by Goldthwait and receiving widespread attention following the studies of Schmorl, has been associated by many writers with the narrowed appearance of the disc as noted on the roentgenogram.

Anterior displacement of the fifth lumbar vertebra on the sacrum, usually associated with a defect in the interarticular portion of the neural arch, has been well described by Neugebauer, Junghanns, Meyer-Burgdorff, and many others. An excellent résumé by Chandler emphasizes that the cause of the cleft in the neural arch and of the forward displacement is as yet undetermined. Numerous observers have recorded the relationship between this condition and the development of low back and sciatic pain. Spondylolysis, prespondylolisthesis and potential spondylolisthesis are the terms used to designate a defect in the arch without forward slipping. Pseudospondylolisthesis is meant to convey forward displacement without defect in the neural arch and presumably due to anomalous articular facets or developmental abnormality in the arch of the fifth lumbar vertebra characterized by prolongation without interarticular defect.

More recently, a condition of posterior displacement of the fifth lumbar vertebra on the sacrum, so called reversed spondylolisthesis, has been described by Smith, Johnson, Williams, Ferguson, and Haggart. These observers have noted the condition to exist frequently in patients with low back and sciatic pain and consider it a common lesion associated with anomalous development or degenerative change of the lumbosacral articular facets and often with narrowed lumbosacral disc.

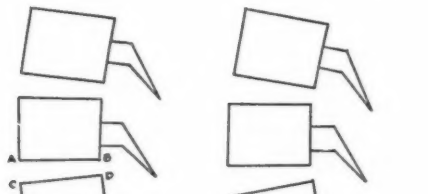

Fig. 1. Schematic drawing of lumbosacral articulation. a, left, Usual relationship fifth lumbar and sacrum. b, right, Anterior displacement fifth lumbar vertebra with defect in neural arch.

The existence of this condition has, however, been vigorously denied by Willis on the basis of anatomical studies. He believes that the appearance on the roentgenogram is always due to the larger anteroposterior diameter of the fifth lumbar vertebra which creates on the film the optical illusion that it is posteriorly displaced on the sacrum. In skeletons, in 66 per cent of a series of 50 cases, the diameter of the fifth lumbar was greater than the sacrum and in the remainder the measurements were equal. Willis feels that this is an anatomic variation and of no clinical significance. His views are shared by many clinical observers so that the existence of this entity remains controversial.

PURPOSE

In view of the continued difference of opinion relating to the importance of narrowed fifth lumbar disc and displaced fifth lumbar vertebra in the etiology of backache and sciatic pain, a study of a large series of roentgenograms was made with the purpose of establishing the incidence of these conditions. The group of patients whose roentgenograms were reviewed presented themselves for study chiefly because of back and leg complaints. There was, however, a relatively small number whose lumbosacral films were made not for backache but because of pelvic and abdominal conditions, vague extremity complaints and general disorders in which bone changes were suspected. Only one requirement was imposed—satisfactory anteroposterior and lateral lumbosacral films, with a spot lateral in which the central rays passed directly through the lumbosacral joint. Five hundred such films were examined and the authors knew nothing about the reasons for roentgenographic study so that there were included both cases with back and leg pain and also a group with neither of these symptoms.

After determination of the incidence of narrowed lumbosacral disc and displaced fifth (and fourth) lumbar vertebrae, the patients showing these changes on the roentgenograms were studied clinically to determine their principal complaints and important physical findings in the hope that this would throw some light on the importance of these roentgenographic changes. One hundred eighty-one cases were so studied. For comparison, the clinical findings of the 319 patients whose films showed no displacement or narrow disc were also reviewed.

ROENTGENOLOGIC STUDY

The method of investigation of the true lateral roentgenograms is demonstrated diagrammatically in Figures 1 and 2. The anterior and posterior fourth lumbar disc measurements are designated by *AC* and *BD*, respectively, while these measurements for the fifth lumbar disc are represented by *EG* and *FH*. The anteroposterior diameters of the fifth lumbar and first sacral segments are measured respectively as *EF* and *GH*. Anterior displacement of the fifth lumbar vertebra measured at the posterior border is represented by *H'H*, whereas posterior displacement measured at the posterior border is *HH'*. In a previous article one of the authors (EAB) in the study of a series of roentgenograms of backache and control cases established an arbitrary minimum normal posterior fifth lumbar disc measurement as 5 millimeters. In this series all fourth or fifth lumbar posterior disc measurements less than 5 millimeters were considered narrow. Other observations from the true lateral views were the incidence of lumbosacral arthritis, flattening of the lumbar spine, and

increased lumbar lordosis. Defects in fifth lumbar neural arch were observed and recorded.

In the anteroposterior lumbosacral films, transitional lower lumbar vertebrae were noted, together with other lumbosacral anomalies such as separate neural arch and spina bifida occulta. Immature, horizontal, or grossly abnormal lumbosacral facets were recorded in their relationship to fifth lumbar displacement. When a transitional lower lumbar vertebra was observed on the anteroposterior film, care was taken to avoid measuring the transitional disc on the lateral view as the lumbosacral disc. When a sacral vertebra was *completely* lumbarized, the sixth lumbar disc was considered the lumbosacral. When a fifth lumbar vertebra was *completely* sacralized the fourth lumbar disc was considered the lumbosacral. In cases of *partial* lumbarization or sacralization, the disc immediately above the transitional vertebra was considered to be the lumbosacral. Although we did not have films of the complete spine and there may have been occasional error due to uncertainty as to which vertebra was the first lumbar, it is felt that the error was minimal and certainly in no case was a transitional lower lumbar disc recorded as a narrow lumbosacral disc. The authors are furthermore well aware of the obvious lack of precision in the measurement of roentgenograms, especially since there is always some slight difference in positioning and technique. However, it is felt that this lack of precision is well distributed in the large series and from the practical point of view can be disregarded in the interpretation of the roentgenologic findings.

Statistical Study of Roentgenograms

Narrow disc. Of the five hundred roentgenograms there was definite narrowing of the fifth lumbar disc at the posterior margin in 132 (26.4%). The fourth lumbar disc was narrowed posteriorly in 18 (3.6%). The latter was associated with narrow fifth lumbar disc in 13 (2.6%).

The relative size of the fourth and fifth lumbar discs was studied. In the case of the *anterior* disc measurements the fourth lumbar was greater than the fifth in 184 (36.8%), it was less than the fifth in 256 (51.2%) and the measurements were the same in 60 (12.0%). In the case of the *posterior* disc measurements the fourth lumbar was greater than the fifth in 388 (77.6%), it was less than the fifth in 54 (10.8%), and the measurements were the same in 58 (11.6%).

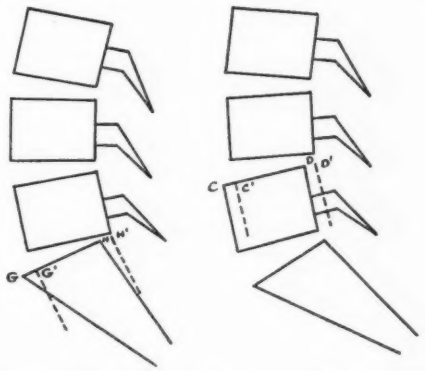

Fig. 2. Schematic drawing of lumbosacral articulation. a, left, Posterior displacement fifth lumbar vertebra and narrowed fifth lumbar disc; b, right, posterior displacement fourth lumbar vertebra.

Figure 3 shows the relative size of the fourth and fifth lumbar disc measurements. On the average, *AC* is somewhat less than *EG*, but *BD* is considerably greater than *FH*. This would tend to show that there is a greater strain placed at the lumbosacral joint than in the region of the fourth lumbar articulation and might be one of the factors in the greater incidence at this point of strain, degenerative change, narrowed intervertebral foramina and

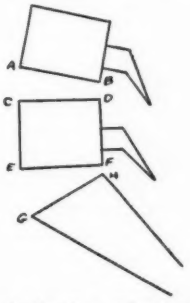

Fig. 3. Schematic drawing of lumbosacral articulation showing difference in fourth and fifth lumbar disc measurements and possible relationship to the frequency of lumbosacral pain. *AC<EG; BD>FH. AC:BD::2.5:1. EG:FH::3.4:1.*

possibly posterior disc protrusion. In support of this hypothesis an average of the fourth and fifth lumbar disc measurements in the series shows that the relationship between *AC* and *BD* is 2.5 to 1, whereas the relationship between *EG* and *FH* is 3.4 to 1.

Displacement of Fifth Lumbar Vertebra

Displacement of the fifth lumbar vertebra occurred in this series in 76 (15.2%). Of these cases 32 (42.3%) were associated with narrow fifth lumbar disc.

Posterior displacement of the fifth lumbar occurred in 51 (10.2%). Of these 24 (43.1%) were associated with narrow disc. Anterior displacement of the fifth lumbar occurred in 25 (5.0%) and of these 8 (32.0%) were associated with narrow disc.

Anterior and posterior displacements were measured at both the anterior and posterior edges. In this series the *average* anterior displacement of the fifth lumbar vertebra at the anterior edge was 5.0 millimeters (L 16 S2), while at the posterior edge it was 5.4 millimeters (L 14 S 2). In the case of posterior displacement of the fifth lumbar, the *average* posterior displacement at the anterior edge was 2.2 millimeters (L 5 S 0), while at the posterior edge it was 4.6 millimeters (L 8 S 2).

Anteroposterior diameters. In considering the general question of displacement of the fifth lumbar vertebra, the relative depth of the fifth lumbar and first sacral segment was studied. In the entire series the anteroposterior diameter of the fifth lumbar was greater than that of the first sacral in 236 (47.2%), while it was less than the first sacral in 112 (22.4%). The measurements were the same in 152 (30.4%).

In cases showing posterior displacement of the fifth lumbar vertebra the diameter of this vertebra was greater than that of the first sacral in 47 (92.2%), less than the first sacral in none, and the same in 4 (7.8%).

In cases showing anterior displacement of the fifth lumbar vertebra the diameter of this vertebra was greater than the first sacral in 6 (24%), less than the first sacral in 14 (56%), and the same in 5 (20%).

It will be noted that in posterior and anterior displacement of the fifth lumbar vertebra, there is a reversal of the relative number of cases in which the anteroposterior diameter of the fifth lumbar is greater than that of the first sacral. In the cases with posterior displacement the percentage of these cases is approximately twice that of the entire series, whereas in anterior displacement it is approximately half that percentage.

Apparent cause of displacement. Because it has been suggested that difference in anteroposterior diameters of the fifth lumbar and first sacral segments might account for the appearance of posterior displacement (and also presumably for some cases of apparent anterior displacement), each film showing anterior or posterior displacement was carefully evaluated from this point of view. Only the posterior edges were used in this evaluation because measurement of displacement at the anterior edge is extremely inaccurate, and it has been shown by Ferguson that there is anterior lipping and compensatory increase in anteroposterior diameter of the first sacral segment as a result of the abnormal pressure on the anterior sacral edge in spondylolisthesis.

Comparison was made between the difference in anteroposterior diameters of the fifth lumbar and first sacral segments and the amount of displacement as measured at the posterior edge of these segments. If the difference in diameters was exactly the same as the amount of displacement, it was assumed that the appearance of slipping was due to the difference in diameters alone. If there was no difference in diameters the amount of displacement was assumed to be a true forward or backward slipping. If there was a difference of diameters, but this was not as great as the amount of displacement, it was assumed that the displacement was due to a combination of difference in diameters and true forward or backward slipping.

In cases with posterior displacement, the difference in diameters alone could account for the apparent displacement in 10 (19.6%). Posterior slipping alone was the apparent cause in 4 (7.8%), while a combination of the two factors was noted in 37 (72.6%).

In cases with anterior displacement, the difference in diameters alone was the apparent cause in none. Anterior slipping alone was re-

Fig. 4. Roentgenogram of anterior displacement fifth lumbar vertebra. Lateral view showing defect in neural arch.

Fig. 5. Anterior displacement fifth lumbar vertebra. Lateral view with no defect in neural arch. Oblique views also showed no defect.

sponsible in 11 (44.%), while a combination of the two factors was noted in 14 (56.0%) instances.

Fifth Lumbar Arch Defects

Since it is a common observation that there is almost always a defect in the interarticular portion of the fifth lumbar neural arch to account for anterior displacement while no such logical explanation can be given for posterior displacement, the presence of such defects was observed and recorded (Fig.4). It is also conceivable that either anterior or posterior displacement might be due to anomalies or degenerative changes in the lumbosacral articular facets.

In the 25 cases of anterior displacement of the fifth lumbar vertebra, a definite defect in the neural arch was noted in 21 (84%). In none of these cases was anything unusual noted in the lumbosacral facets. In 3 cases (12%), no break in the arch was observed, but since no oblique views of the lumbosacral area were available in these cases it must be assumed that the defect might have been revealed by such views. In only 1 case (4%) was there definite anterior displacement with no defect on any of the lumbosacral views, despite repeated examination (Fig. 5). This case did show immature lumbosacral facets.

The anterior edge of the sacrum was studied in these cases of anterior displacement to note the presence of anterior lipping and spur formation. It was felt that this factor might account for the increased percentage of cases in this group which showed the anteroposterior diameter of the first sacral segment to be greater than that of the fifth lumbar. In 11 cases (44%) definite anterior spur formation was noted.

Fig. 6. Posterior displacement fourth lumbar vertebra, lateral view. There is old healed osteomyelitis of the second, third, and fourth lumbar vertebrae.

Fig. 7. Narrow fifth lumbar intervertebral disc. Lateral view showing the presence of associated arthritic changes.

In the cases of posterior displacement, the cause was investigated from the appearance of the lumbosacral articular facets. In only 5 cases (10%) was there any suggestion from the roentgenogram that immature, horizontal or completely internal-external facets might be the basic factor in the displacement.

Fourth Lumbar Displacement

Displacement of the fourth lumbar vertebra was noted posteriorly in 13 (2.6%) (Fig. 6) and anteriorly in 2 (0.4%). This was noted in association with fifth lumbar displacement in 8 (1.6%). The *average* anterior displacement at the anterior edge was 4 millimeters (L 5 S 3) and at the posterior edge was 4 millimeters (L 5 S 3). The *average* posterior displacement at the anterior edge was 2.2 millimeters (L 5 S 0) and at the posterior edge was 3.8 millimeters (L 5 S 3). The anterior cases were accompanied by a definite break in the neural arch of the fourth lumbar vertebra.

Lumbosacral Region

Anomalies. The total cases with lumbosacral anomalies consisting of transitional lower lumbar vertebrae, spina bifida occulta, defective neural arch, and immature articular facets were 165 (33%).

Transitional lower lumbar vertebrae were noted in 69 (13.8%). Of these cases there was an associated narrow lumbosacral disc (*not* immature transitional disc) in only 9 (13%). Complete lumbarization was noted in 23 (4.6%) and partial lumbarization in 38 (7.6%). Complete sacralization was present in 7 (1.4%) and partial sacralization in 1 (0.2%).

The other lumbosacral anomalies were noted in 112 (22.4%) and of this number 16 (14.3%) were associated with transitionals and 30

(26.8%) were associated with narrow fifth lumbar disc.

Arthritis. Definite arthritic changes were noted at the lumbosacral articulation in 36 (7.2%). Of these 25 (70%) were associated with narrow fifth lumbar disc (Fig. 7).

Of 181 cases with narrow disc or lower lumbar displacement, 27 (15.0%) had lumbosacral arthritis. This was present in only 2.8% of the other cases in the series.

Curve. There was definite loss of the normal lumbar curve in 62 (12.4%). It is noteworthy that in the 51 cases of posterior displacement of the fifth lumbar vertebra the lumbar curve was flat in 16 (31.4%), whereas in anterior displacement it was flat in only 1 case (4%). Of the cases with flat lumbar spine there was associated narrowed fifth lumbar disc in 21 (34.0%).

Of 181 cases of narrow disc or displacement, 27 (15.0%) had flat lumbar spine. This was present in 11.0% of the other cases.

Increased lumbar lordosis was noted in 16 (3.2%). In the cases with anterior displacement of the fifth lumbar vertebra increased lordosis was present in 3 (12.0%), while in posterior displacement it was noted in none. Of the cases with increased lumbar lordosis there was associated narrowed fifth lumbar disc in 4 (25%).

Of 181 cases of narrow disc or displacement, 8 (4.4%) had increased lordosis. In the other cases it was found in 2.5 per cent.

CLINICAL STATISTICS

The clinical records of the patients were examined after the roentgenographic findings had been recorded. Most of the patients had been seen by the senior author in consultation and his clinical findings noted on the records.

There were 181 patients (36.2%) whose roentgenograms showed narrow fifth lumbar disc, displacement of the fourth or fifth lumbar vertebra or a combination of these findings. There were 319 patients (63.8%) whose films showed none of these changes. The latter will be referred to as the control group.

The patients were chiefly adult males. There were 176 (97.3%) between the ages of 21 and 60. Only 1 patient was under 21 years and 4 were over 60 years.

Fig. 8. Posterior displacement fifth lumbar vertebra, lateral view. The slight difference in anteroposterior diameters of the fifth lumbar and first sacral segments only partially accounts for the amount of posterior displacement.

Incidence of Back Pain

Of the entire series of 500 patients, backache was present in 405 (81.0%), there was associated leg pain in 145 (29.0%) and neither of these complaints was recorded in 95 (19.0%). In no case was there leg pain alone, although in a few the complaint of hip pain was interpreted as backache.

Of the 181 patients with narrow disc or lower lumbar displacement, backache was present in 153 (84.5%) and there was associated radiating leg pain in 53 (29.2%). In 28 (15.5%) neither of these complaints was present.

In the control group backache was present in 252 patients (79%), there was associated leg pain in 92 (29%), and in 67 (21%) neither complaint was noted.

Conversely, there were in the entire series 260 patients with back pain alone. Of these,

TABLE I.—INCIDENCE OF NARROW 5TH LUMBAR DISC AND LOWER LUMBAR DISPLACEMENT

	Entire series	Patients with back pain alone	Patients with back and leg pain	Neither back nor leg pain
No. of cases	500	260	145	95
	Per cent	Per cent	Per cent	Per cent
Narrow 5th L. disc	26.4	27.3	26.2	24.2
Posterior displacement 5th L. vertebra	10.2	10.8	12.4	5.3
Anterior displacement 5th L. vertebra	5.0	5.4	5.5	3.2
Displacement 4th L. vertebra	3.0	3.5	4.1	0.0
Combinations of above	36.2	38.5	36.6	30.0

100 (38.5%) were associated with narrow disc or lower lumbar displacement on the roentgenograms. There were 71 (27.3%) with narrow fifth lumbar disc, 28 (10.8%) with posterior fifth lumbar displacement, 14 (5.4%) with anterior lumbar displacement, and 9 (3.5%) with fourth lumbar displacement.

There were 145 patients with back and leg complaints. Of these, 53 (36.6%) were associated with narrow disc or lower lumbar displacement on the films. There were 38 (26.2%) with narrow fifth lumbar disc, 18 (12.4%) with posterior fifth lumbar displacement, 8 (5.5%) with anterior fifth lumbar displacement and 6 (4.1%) with fourth lumbar displacement.

There were 95 patients who complained of neither back nor leg pain. Of these, 28 (30.0%) were associated with narrow fifth lumbar disc or displaced lower lumbar vertebra on the films. There were 23 (24.2%) with narrow disc, 5 (5.3%) with posterior fifth lumbar displacement, 3 (3.2%) with anterior fifth lumbar displacement, and none (0.0%) with fourth lumbar displacement. The relationship between these clinical and roentgenographic findings is represented in Table I.

Clinical Study of Backache Cases

Leg pain. Of the 153 narrow disc and displacement cases with back pain there was associated leg pain in 53 (34.6%). Of the cases with leg pain 51 (96.2%) were in the sciatic distribution. The remainder were in the region of the anterior thigh.

Of the 252 control patients with back complaints, 92 (36.5%) had leg pain, and of these 80 (86.0%) were in the sciatic distribution.

Of the cases of anterior displacement of the fifth lumbar, 8 (32%) had sciatic pain. In the posterior displacement cases, 16 (31.4%) and in the fourth lumbar displacement, 3 (20%) had sciatic radiation.

Altered Achilles reflexes. In the series of 153 patients there was alteration of the Achilles reflex in 15 (9.8%), the reflex being diminished in 7 (4.6%) and absent in 8 (5.2%). In 100 of these cases with back pain alone there was alteration in the Achilles reflexes in 6 (6.0%), whereas in the 51 patients with sciatic pain these reflexes were altered in 9 (17.7%).

In the 252 control cases, there was alteration in leg reflexes in 22 (8.7%), absence in 16 (6.3%) and diminution in 6 (2.4%).

In the cases of posterior fifth lumbar displacement alteration of reflexes was noted in 3 (6%), while this was present in none of the cases of anterior displacement. In fourth lumbar displacement altered Achilles reflexes were present in 2 (13.3%).

Straight leg raising. Of the 153 cases limited, painful straight leg raising was present in 29 (19%). This was unilateral in 19 (12.4%) and bilateral in 10 (6.6%).

Of the 252 control cases, limited straight leg raising was noted in 45 (17.8%). This was unilateral in 38 (15.1%) and bilateral in 7 (2.7%).

In cases with posterior displacement of the fifth lumbar, limited straight leg raising was present in 8 (16%). In anterior displacement it was noted in 1 (4.0%). In displacement of the fourth lumbar vertebra this sign was positive in 3 (20%).

Body list. A list of the body to one side in the erect position, or a shift to one side on forward bending was noted in 12 patients (7.8%). This occurred toward the side of pain in 7 (4.6%) and away from the side of pain in 5 (3.2%).

In the 252 control cases, tilt of the body on bending was noted in 13 cases (5.0%). This occurred toward the side of the pain in 10 (3.9%) and away from it in 3 (1.1%).

Symptom-free cases. Of the 181 cases with narrow disc or displacement there were 28 patients who presented no back or leg complaint.

Of 132 cases with narrow fifth lumbar disc 23 (17.4%) had no complaints. Of 51 cases with posterior displacement of the fifth lumbar 3 (5.9%) were without back or leg pain and of 25 cases of anterior displacement 2 (8%) did not make these complaints. Of 15 cases of displacement of the fourth lumbar vertebra all presented symptoms of backache with or without leg pain.

Diagnosis. It is noteworthy that in 20 patients (13.0%) no definite orthopedic diagnosis could be made to account for the patient's back and leg complaints. In the control group, there was failure in diagnosis in 67 (26.6%).

Of the 153 patients with such complaints, 61 (40.0%) were thought to have some form of arthritic change, 50 (32.7%) were thought to have a localized muscular or ligamentous strain, and 16 (10.4%) were diagnosed as a lower lumbar posterior disc protrusion. Other diagnoses were made in 6 (3.9%). There were 4 cases in which the complaints were thought to be due to an old spinal osteochondritis, one was due to a secondary lesion from carcinoma of the prostate and one was due to simple contusion.

In the control group, 41 (16.3%) were diagnosed as arthritis, 106 (42.1%) as strain, 28 (11.1%) as protruded disc, and other diagnoses were 10 (3.9%). A comparison of the clinical findings noted in the group with narrow disc or displacement and in the control group is represented in Table II.

Disc series. Because a narrowed lower lumbar disc on the roentgenogram is often associated by authors with posterior protrusion of such a disc and the production of clinical signs, the cases in which protruded lower lumbar intervertebral disc had been diagnosed were studied with this point in mind. There were 44 patients on whom this clinical diagnosis had been made. Of these, 33 (75%) were diagnosed by clinical methods and 11 (25%) were confirmed by surgical exploration.

In this group the incidence of narrowed lower lumbar disc as noted on true lateral roentgenograms was 13 (30.0%). Of the cases confirmed by operation, 9 revealed protrusion at the fifth lumbar interspace. A review of these films revealed a narrowed fifth lumbar disc in 3 (33.3%). A posterior protrusion of the fourth lumbar disc was revealed at operation in 2 cases. Both of these showed narrowed *fifth* lumbar intervertebral disc on the roentgenograms.

TABLE II.—ROENTGENOGRAPHIC AND CLINICAL FINDINGS

	Narrow disc or displacement 181 cases Per cent	Control group 319 cases Per cent
Lumbosacral arthritis	15.0	2.8
Flat lumbar spine	15.0	11.0
Increased lordosis	4.4	2.5
No back or leg pain	15.5	21.0
Back pain with or without leg pain	84.5	79.0
Back pain alone	55.3	50.0
Back pain with leg pain	29.2	29.0
Clinical findings	153 cases with back symptoms	252 cases with back symptoms
Associated leg pain	34.6	36.5
Sciatic pain	33.3	31.6
Altered reflexes	9.8	8.7
Limited straight leg raising	19.0	17.8
Body tilt	7.8	5.0
No diagnosis	13.0	26.6
Diagnosis—strain	32.7	42.1
Diagnosis—arthritis	40.0	16.3
Diagnosis—disc protrusion	10.4	11.1
Other diagnoses	3.9	3.9

Of the 44 cases, 6 (13.7%) revealed posterior displacement of the fifth lumbar vertebra. Of the 6 cases with posterior displacement, 3 (50%) were associated with narrowed disc. No case of anterior displacement of the fifth lumbar vertebra was noted in this series.

DISCUSSION

Several of the roentgenographic and clinical findings seem worthy of brief discussion. The relationship which has been observed between the fourth and fifth lumbar disc measurements indicates the vulnerability of the lumbosacral articulation to mechanical strain, a point which has been emphasized by numerous observers. Any change in the usual anatomic structure of the lumbosacral joint, such as narrowed fifth lumbar disc, especially posteriorly, and anterior or posterior displacement of the lower lumbar vertebrae, would in all likelihood place additional burden on a point of mechanical weakness and might produce pain in the lower back with or without leg radiation. Whether or not such complaints develop would depend on the ability of the as-

sociated muscles and ligaments to compensate for the exaggerated mechanical strain.

It would appear that posterior displacement of the fifth lumbar vertebra is not uncommon and that it is not usually due solely to a difference in diameters of the fifth lumbar and first sacral segments. The exact cause of such displacement is conjectural and although it is assumed that anomalies of the lumbosacral facets are the basic predisposing factors, the roentgenograms offer no satisfactory evidence for this hypothesis.

Anterior displacement of the fifth lumbar vertebra occurs with half the frequency of posterior displacement and is almost always associated with a defect in the neural arch. In 44 per cent of cases there is compensatory lipping of the anterior edge of the sacrum.

Comparison of the anteroposterior diameters of the fifth lumbar and first sacral segments in attempting to explain the appearance of posterior fifth lumbar displacement on the roentgenogram, reveals that the fifth lumbar diameter in the entire group is greater than the first sacral in approximately 50 per cent. Where there is posterior fifth lumbar displacement, however, the fifth lumbar diameter is greater in about 90 per cent, and where there is anterior fifth lumbar displacement it is greater in only about 25 per cent. Since it is known that anterior lipping of the sacrum is present very often in cases of anterior displacement and this might account for greater anteroposterior sacral diameter in these cases, it would seem reasonable to consider, in cases of posterior displacement, the possibility of secondary *atrophy* of the anterior edge of the sacrum which would account for the lessened anteroposterior sacral diameter in this group.

The similarity between the clinical findings in the groups with and without narrow fifth lumbar disc and lower lumbar displacement is most striking. Since the incidence of back pain, leg pain, altered reflexes and limited straight leg raising is the same in the two groups, it would appear that in most cases narrow disc and lower lumbar displacement are not in themselves the cause of symptoms. This is reinforced by the similarity of incidence of narrow disc and lower lumbar displacement in cases with back pain alone, with back and associated leg complaints, and in cases presenting neither of these symptoms. Only in the case of fifth lumbar displacement is there a different incidence in the groups with and without symptoms.

It is remarkable that the incidence of back and leg pain was the same in the two groups in spite of the fact that there was a much higher percentage of cases with lumbosacral arthritis in the patients with narrow disc and displacement. It might be deduced from this what has often been suspected; namely, that localized changes noted on the roentgenograms are not necessarily the cause of the patient's complaints. The greater frequency of arthritic change in the one group, however, would tend to confirm the belief that narrow disc and lower lumbar displacement cause increased lumbosacral strain and that such patients are more likely to develop decompensation of muscular and ligamentous structures as the result of acute or chronic trauma than are patients without these anatomic variations.

From the study of cases in which a diagnosis of ruptured nucleus pulposus or posterior disc protrusion was made, it is apparent that the incidence of narrow fifth lumbar disc is no greater in this group than in other patients. Such an x-ray finding cannot, therefore, be used as clinical evidence of disc protrusion.

From the roentgenographic and clinical data which have been accumulated, it would seem that narrow fifth lumbar disc and lower lumbar displacement occur with similar frequency in patients with or without symptoms, that there is no characteristic clinical syndrome which they present and that they are not in themselves the cause of backache and leg pain. However, like other lumbosacral anomalies, they may further weaken the lumbosacral articulation and make it even more susceptible to injury.

This study has thrown no light on the etiology of these lower lumbar anomalies. Undoubtedly some are due to congenital defects, some to developmental changes, and others to the effect of acute and chronic trauma, but unless followed by muscular or ligamentous decompensation they are not necessarily productive of symptoms and are of no significant clinical importance.

SUMMARY

1. In a series of 500 roentgenograms focused over the lumbosacral joint, narrowed fifth lumbar disc was noted in 26.4 per cent, posterior displacement of the fifth lumbar vertebra was present in 10.2 per cent, anterior displacement of the fifth lumbar was present in 5.0 per cent, and there was displacement of the fourth lumbar vertebra in 3.0 per cent.

2. The incidence of back and leg pain in the 181 cases in which these changes were noted was not significantly greater than the incidence of these complaints in the other 319 cases.

3. When the two groups were studied clinically, they showed a strikingly similar incidence of alteration in leg reflexes, limitation of straight leg raising, and body tilt on forward bending.

4. The clinical diagnoses in the two groups were almost identical. There was, however, a considerably higher incidence of lumbosacral arthritis in the patients with narrow disc or lower lumbar displacement.

5. A study of the groups of patients with back pain alone, with associated leg pain, and with neither of these complaints revealed no significant difference in the incidence of narrowed fifth lumbar disc, but there was a smaller incidence of lower lumbar displacement in the symptom-free group.

6. Posterior displacement of the fifth lumbar vertebra is apparently a definite entity and is not due entirely to difference in anteroposterior diameters of the fifth lumbar vertebra and the sacrum, although in about 20 per cent this is apparently the reason for the appearance on the roentgenogram. It is possible that in cases of posterior displacement, there is secondary atrophy of the anterior edge of the sacrum which decreases the anteroposterior diameter of the first sacral segment.

7. Anterior displacement of the fifth lumbar vertebra is usually associated with a defect in the interarticular portion of this vertebra and in at least 40 per cent of the cases there is anterior lipping of the sacrum which increases the anteroposterior diameter of the first sacral segment.

8. In cases of herniated nucleus pulposus or posterior disc protrusion, the incidence of narrowed fifth lumbar disc or lower lumbar displacement is not significantly greater than in the remainder of the series. Narrow disc on the roentgenogram cannot be considered clinical evidence of posterior disc protrusion.

9. Narrowed fifth lumbar disc and displacement of the lower lumbar vertebrae are clinically significant only in that these conditions place additional strain on an already mechanically vulnerable lumbosacral joint.

10. The weight of evidence seems to indicate that in most instances narrow fifth lumbar disc and lower lumbar displacement are in themselves not the cause of low back and sciatic pain. As is true in the case of transitional vertebrae and other lumbosacral anomalies, the presence or absence of back or leg pain depends almost entirely upon the integrity of the surrounding muscular and ligamentous structures. So long as these structures are intact, the patient may be symptom-free. When they are no longer able to compensate for the abnormal mechanical strain, pain may occur because of tension on muscle and ligamentous attachments, degenerative arthritic changes in the articular facets or actual pressure on the spinal nerves at some point in the region of the deranged lumbosacral articulation.

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A CORRELATION OF NEUROLOGIC, ORTHOPEDIC, AND ROENTGENOGRAPHIC FINDINGS IN DISPLACED INTERVERTEBRAL DISCS

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ALTHOUGH the number of operations for displaced intervertebral disc has been steadily increasing, comparatively few surgeons have published thorough reviews of their postoperative results. There remains considerable difference of opinion as to the precise indications for operation, the most favorable type of operation, and whether or not a primary or secondary fusion should be attempted. Most reports have been limited to the problem of subjective improvement of back and sciatic pain and the objective neurologic changes following operation. Some authors have also attempted to correlate the effect of trauma and occupation with the etiology and degree of postoperative improvement (4, 8). Occasional papers have considered the result from an orthopedic or radiologic viewpoint (2, 3).

The purpose of this paper is to present a group of postoperative disc patients who have been critically studied neurologically and orthopedically. The results of these examinations were then integrated with the roentgen findings. In this way we hoped to determine any relationship that might exist between the preoperative and postoperative roentgenograms, the operative findings, and the eventual operative result.

For the purpose of this review a group of 95 postoperative intervertebral disc patients was collected from the Neurosurgical Service of the Hospital of the University of Pennsylvania. This series consisted only of patients operated upon for displaced lumbar intervertebral discs.

The follow-up study consisted of a careful physical examination by members of the orthopedic and neurosurgical staffs. This was followed by anteroposterior and lateral roentgenograms of the lumbar spine and pelvis. Neurologically, the patients were examined for sensory, motor, and reflex changes. The lower limbs were checked for signs of atrophy or weakness and for the presence of pain on straight leg raising. Orthopedically, the patients were examined for any scoliosis, restricted mobility, paravertebral spasm, or pelvic tilt. All patients were questioned as to the presence of any residual back pain or sciatic pain. Finally, the patients were asked concerning their personal opinion of the operation. Each patient was asked if he was fully satisfied with the results of the operation and the results recorded as "yes," "no," or "questionably satisfied." The preoperative and postoperative findings were carefully compared and the preoperative and postoperative roentgenograms reviewed by a member of the radiology staff. An attempt was made to correlate the x-ray findings with the postoperative physical findings in each case. A special study was made of those patients who were definitely not, or only questionably, satisfied.

The patients were divided into two main groups, of laborers and non-laborers, since it was felt that this difference in occupation might have a bearing on the etiology and the result. Also, the possibility of trauma was listed in each case. The follow-up period varied from less than 1 year to more than 5 years. The patients were divided into four groups as follows: less than 1 year (16 patients), 1 to 3 years (30 patients), 3 to 5 years (32 patients), and over 5 years (17 patients). Postoperative findings at operation were, likewise, divided into subgroups. Discs were listed as ruptured, protruded, or hidden. In the remaining cases findings of hypertrophied ligamentum flavum or negative exploration were listed as such.

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The type of operation seemed an important factor. Accordingly, the operations were divided into three groups: laminectomy, hemilaminectomy, and interlaminal dissection.

Indications for operation have varied somewhat over the years since this subject first came into prominence. During the past 4 years, however, we have become more conservative and have felt that the results were more gratifying from both the patient's and our own point of view. We first use conservative therapy in the form of rest and board mattress. Buck's extension for 10 to 14 days follows, and the patient is sent home with a brace or supportive belt. There is a decided advantage if the patient has had several recurrent bouts of severe pain before operation is eventually decided upon. If operation is performed when the patient has little or no back or leg pain, the distress resulting from the operative incision may well make him feel that his condition has not been improved by surgery. But if his pain, particularly his leg pain, has been acute and is promptly relieved by removal of the disc, he is quite willing to put up with the postoperative back pain. He feels that he has been definitely improved by surgery. His attitude with regard to the final operative result is optomistic, a very important factor in obtaining satisfactory relief. Due to this preoperative conservatism, we believe that we have increased both our proportion of ruptured discs found at operation and the percentage of satisfied patients. At present, whenever possible, the routine disc operation consists of an interlaminal dissection. Postoperatively, weight-bearing is permitted on the fifth to seventh day provided the patient has a light supportive belt. This we advise wearing for the first 6 weeks to 3 months. It is then to be discarded gradually as the patient increases his activities.

ETIOLOGY

The etiology of the displaced nucleus pulposus has remained an interesting question. The preponderance of male sufferers and the percentage of patients with a history of injury suggest a traumatic origin.

Of the 71 males and 24 females comprising the group studied, 56 per cent claimed a traumatic onset. It is of interest to note that almost as many non-laborers traced their disability to a traumatic incident as laborers. Half of the laborers remembered no one precipitating event.

The operative findings revealed that in the nontraumatic group 21 per cent showed indefinite findings such as hidden disc, hypertrophied ligamentum flavum, or no findings at all, compared to only 13 per cent showing such indefinite findings in the traumatic group.

The majority of the patients were in their third and fourth decades, the youngest being 19 and the oldest 63. Patients complained of back pain preoperatively for an average period of 5 years and sciatic pain for an average period of 2¾ years.

DIAGNOSIS

While the determination of the presence or absence of a ruptured disc depends, for the most part, on physical and neurologic findings, other diagnostic aids are frequently used. In order to ascertain the reliability of some of these aids, a study was made of the spinal fluid protein level, conventional x-rays, and myelography.

In 54 patients a spinal fluid protein was determined preoperatively. Forty-eight per cent of the readings were below 50.0 milligrams per cent while 43 per cent were between 50.0 and 100 milligrams per cent. In 9 per cent there were values over 100. These results indicate the doubtful value of the spinal protein in establishing a diagnosis.

The conventional roentgen examination consisted of an anteroposterior projection of the pelvis and lumbar spine and a lateral projection of the lumbar and lumbosacral spine. This type of examination was made in 68 patients preoperatively. In such conventional films preoperative roentgen changes were found in approximately one-half of these patients. We do not believe that there is any absolute correlation between such findings and the presence of a displaced intervertebral disc or hypertrophied ligamentum flavum since an equal number of patients in this age group who do not have such disease will show similar roentgen changes. However, appreciable narrowing of an intervertebral space indicates loss

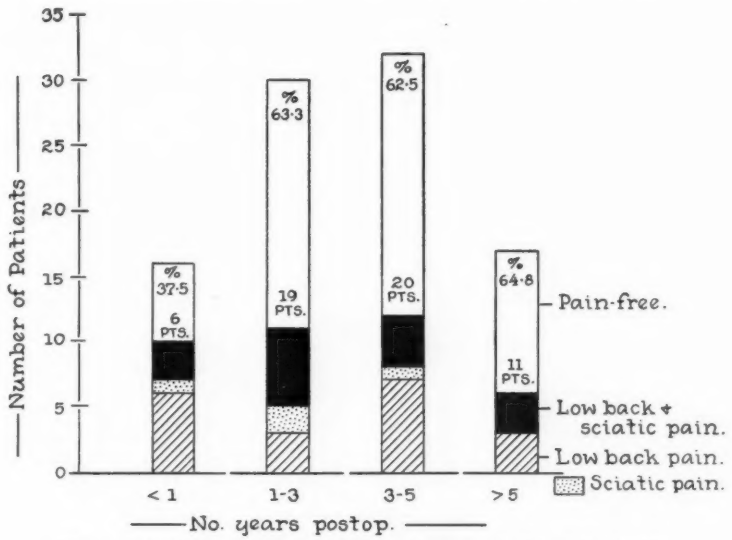

Fig. 1. Relationship of postoperative time interval to back and sciatic pain.

of substance of the disc either by degeneration and absorption or by extrusion. When this is found in a patient with the usual clinical syndrome, we feel that it should be considered as corroborative evidence.

The changes seen in conventional preoperative roentgen examinations in 68 patients are reviewed in the light of operative findings.

Air myelographic studies were made in 15 patients of the series. Opaque myelographic studies were made in 61 patients of the series; in 39, pantopaque was used, and in 22, lipiodol. At the conclusion of the examination an attempt was made to remove the oil under fluoroscopic guidance in 45 of the 61 patients so examined.

The correlation of air myelograms with operative findings in 15 patients indicates that when a filling defect in the air column was found, surgical exploration was positive. The absence of a defect in an air myelogram, however, could not be considered as conclusive evidence that a lesion was not present.

From correlation of oil myelograms with operative findings in 61 patients it is evident, as others have also shown, that a high degree of accuracy is obtained in oil myelography. In this series a differential diagnosis was not made between hidden disc, protruded disc, ruptured disc, and hypertrophied ligamentum flavum. The oil myelograms showed defects which appeared similar in these four conditions.

RESULTS

As previously indicated, the 95 patients seen postoperatively were divided into four groups for evaluation. The follow-up periods ranged from less than 1 to over 5 years. When the patient was asked to evaluate his own result and whether or not he was fully satisfied and would again elect operation for his original complaints, knowing in advance what relief he could anticipate, 83 or 87 per cent of the patients replied in the affirmative. Seven per cent claimed they were dissatisfied, and 5 patients (5 per cent) could not decide. All of the discs operated upon in this series were between the fourth and fifth lumbar or the fifth lumbar and first sacral.

More detailed inquiries showed that there were 38 patients (40 per cent) who had residual or recurrent pain. This pain was not sufficiently incapacitating to invalidate the operation in the opinion of the patient. Complaints varied from occasional mild backache in 18 patients or sciatic pain in 4 to those with both

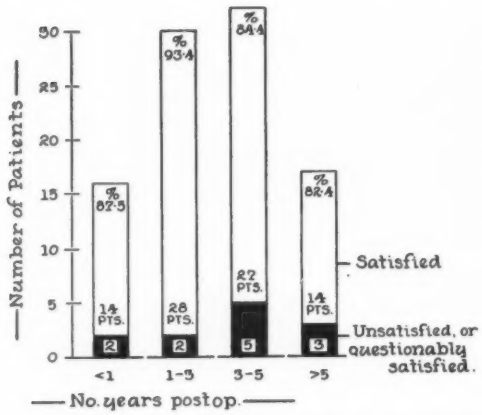

Fig. 2. A comparison of percentage of satisfied patients in various postoperative periods.

low back and sciatic pain present in 16. The largest number of these patients dated the onset of their pain to the operative period. A few claimed a recurrent type of pain originating 1 to 5 years postoperatively.

An analysis of the type of pain in the different follow-up groups showed that a large number of low back complaints occurred in the patients most recently operated upon (Fig. 1). Complaints of low back pain associated with sciatic pain remain at a relatively constant level in each group.

Many diverse complaints of a mild nature were noted. Foremost among these was the presence of annoying muscular cramps in the hamstring and calf muscles on the side of the previous sciatica. Other patients noted low thresholds of back fatigue and subjective hypesthesias, while a foot drop persisted in 1 patient.

An effort was made to determine which operative procedures gave the best results. Surprisingly enough there was no clear cut statistically significant choice between laminectomies, hemilaminectomies, or interlaminal dissections.

Operative findings sharply influence results. Thirty-nine out of 58, or 70 per cent, of the patients with ruptured discs followed over 1 year were pain free. Four patients (44 per cent) with protruded discs were pain free as were 3 patients (50 per cent) of those with hidden discs. Conversely there were only 6 patients (9 per cent) not satisfied when operative findings had revealed a definite rupture of the disc. Three patients (27 per cent) of those with protrusions were not satisfied, as were 2 patients (22 per cent) of those with hidden discs and 1 patient (50 per cent) of those with no findings at all. All of the 5 patients with hypertrophied ligamentum flavum were satisfied.

Although the presence of mild episodes of postoperative back pain was common in those patients with ruptured discs, there was a low incidence of residual or recurrent sciatic pain. This finding contrasted with a higher incidence of residual or recurrent back pain and sciatic pain in those patients who at operation presented hidden or protruded discs. The possibility of a recurring disc may explain such a return of the original complaint in the protruded and hidden group.

From our studies it appears that absent or diminished tendo achillis reflexes do not often return postoperatively. In 74 instances this reflex was lost or diminished postoperatively on the involved side, and in 5 instances it was lost on the opposite side.

Fifteen among 48 (31 per cent) laborers did not return to their former occupations. They decided that they could not continue in their present work and chose lighter work. Some changed because they did not wish to abuse what they regarded as a weakened back while others changed after a trial at their old job which resulted in pain on doing certain types of heavy work. It is probably true that even a larger percentage than indicated modified their daily work although keeping the same job. Only 4 (9 per cent) out of the 47 nonlaborers felt it necessary to seek other jobs. Five years postoperatively 4 patients (23 per cent) out of 17 still wore supports in the form of canvas belts or braces. All of these patients had complaints.

An analysis of the dissatisfied or questionably satisfied patients was undertaken (Fig. 2). One patient had expectations of recovering from a marked foot drop but no improvement in function followed the removal of the ruptured nucleus pulposus. This correlates with the failure of the achillis reflex to return.

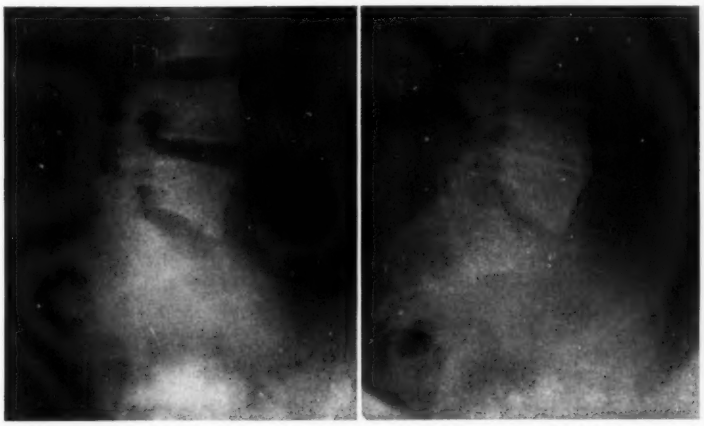

Fig. 3. Preoperative and postoperative films showing marked narrowing and early bridging.

Two patients in whom hidden discs were removed complained of mild residual back pain and sciatic pain. The examination of the back was entirely negative in 1 while some restriction of motion was present in the other. Roentgenograms gave no clues to the causes of these complaints.

Three patients of the dissatisfied or questionably satisfied group had a recurrence of severe sciatic scoliosis, spasm of the erector spinae muscles, and limitation of motion, together with positive straight leg raising tests. This group might show a recurrence of the original pathology. The remaining patients complained of back pain with little explanation afforded for their complaints by physical examination. One of these patients operated upon 6 years ago with x-ray evidence of narrowing of the interspace is relieved by a brace.

Postoperative roentgen studies. A study of the changes seen on the conventional roentgenograms made preoperatively and postoperatively and of the clinical status of the patients reveals that there is no significant relationship between increased narrowing of an intervertebral space and the clinical result. Increased arthritic change is seen in almost exactly the same proportion in the three classified groups of clinical results, and consequently we feel that no significant relationship exists. Fusion or dense, bony bridging between the vertebral bodies above and below the site of the herniated discs is seen in only that group classified as clinically well. It might be presumed that this constitutes a favorable change. It occurred, however, in only 6 of 39, or 15 per cent of the group.

A significant quantity of residual opaque oil was found in 10 of 36 clinically well patients, in 1 of 17 clinically improved patients and in 3 of 8 clinically unimproved patients.

DISCUSSION

Results of other postoperative disc series vary from 24 per cent to 80 per cent cured (4, 5, 7). The present figure of 60 per cent cure compares favorably with these and emphasizes the difference between a straight neurosurgical clinic series and the cross sectional series of Aitken and Bradford. Their cases were reviewed from the files of a large insurance company and reveal a cross section of operative work done by general surgeons, orthopedic surgeons, and neurosurgeons in various clinics throughout the country. They describe their results as excellent (13 per cent), good (17 per cent), and fair (25 per cent). The remaining 45 per cent were graded as "poor" and "bad" results. An excellent result they describe as "no pain and able to return to any type of work." This appears to be the only result comparable with "cure" in other disc series.

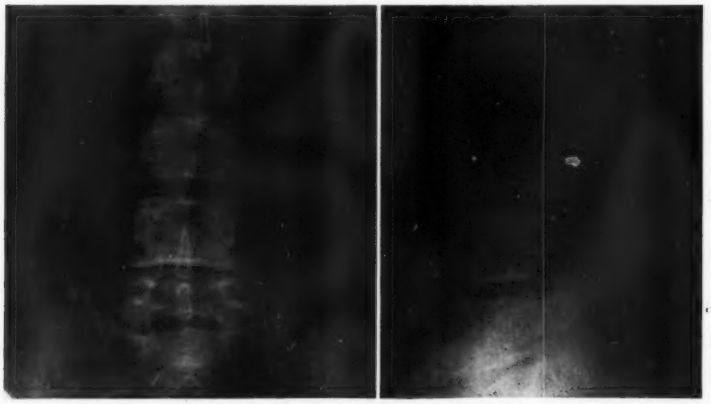

Fig. 4. Normal preoperative films.

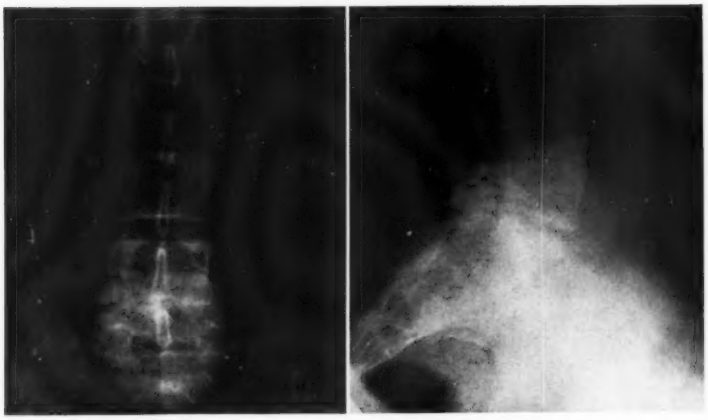

Fig. 5. Postoperative films of the same patient shown in the preceding figure showing narrowing and early fusion.

The results of diagnosis by myelography show the increasing value of this procedure. Begg and Falconer reviewed the myelograms in a series of 86 patients with a disc found at operation. Eighty-eight per cent of these patients showed a positive myelogram for a disc preoperatively while 12 per cent showed a normal myelogram although disc was found at operation. Approximately 66⅔ per cent of their cases showed a laterally displaced disc while 33⅓ per cent were centrally located discs. The discs were almost equally distributed between the fourth and fifth lumbar interspace, although 14 were multiple including 3 at the third lumbar interspace. They recommend exploring centrally displaced discs bilaterally to be sure of complete removal of all ruptured disc material and to avoid a recurrence. Love and Walsh are of the opinion that clinical diagnosis is just as accurate as myelography although they employ air almost routinely preoperatively. There are no definite conclusions on the subject of primary or secondary fusions following disc operations. Aitken and Bradford report on 39 primary fusions performed in their series. Of these 39 cases, 19, or 50 per cent, were able to return to some form of work. There were also

Fig. 6. Preoperative and postoperative films showing narrowing and beginning bony fusion.

15 secondary fusions performed in their series and 9 of these, or 60 per cent, were able to return to some form of work. Love and Walsh believe that cases with frank spondylolisthesis with ruptured disc at the fifth lumbar—first sacral, level usually require a fusion. However, they do not feel that narrowing of an interspace or the presence of spina bifida occulta is an indication for need of fusion. Love, in a recent review of 1,271 postoperative disc patients, questions whether or not fusion of the lumbosacral region causes more stress to be applied at the interspace just above the upper end of the graft with resultant protrusion. In this series he also shows that there is a marked rate of recurrence from less than ½ per cent at the end of 2 years to slightly more than 5 per cent after 5 years postoperatively.

In a group of 843 patients operated on for ruptured disc by the late Walter Dandy, Lenhard was able to examine 147 in a postoperative follow-up. Of these, 23.8 per cent were able to perform their normal activities without complaint. Three types of operation had been employed in this series. Prior to January, 1942, to June, 1943, curettage or removal of the entire disc was done. After June, 1943, multiple discs were recognized and removed entirely. Practically all were done by an interlaminar approach. Analysis of the results showed that there was no relation between the type of operative removal and the degree of cure. He likewise concluded that there is no relationship between a narrowed interspace and the faulty disc, the disc being found either at the level of the narrowed space or at the space above or below. No fusions were done in this series and no myelograms were deemed necessary since 90 per cent were at the fourth or fifth lumbar interspace. Lenhard feels that some of the pateints with residual complaints due to tight muscles or faulty body mechanics could be helped by fusion.

The question of fusion has been closely analyzed by Barr in a series of 234 cases in which patients were operated on for ruptured disc. Of these, 102 had fusion and 132 had been operated upon without fusion. In reply to a questionnaire the same percentage of each group (10 per cent) complained of severe back pain. Likewise the same percentage in each group (63 per cent) stated that they were able to do a full day's work. However, there were 60 per cent of the fused group with no back pain and 45 per cent in the non-fusion group without back pain. Likewise, there were 25 per cent in the fused group that complained of leg pain compared to 46 per cent in the non-fused group with leg pain. He concludes that the trend is toward spinal fusion at the time of laminectomy in an increasing number of cases.

SUMMARY

1. A group of 95 postoperative disc patients was studied by the neurosurgical, orthopedic, and roentgenologic departments.

2. Sixty per cent of these patients were regarded as cured and were able to pursue a normal full day's work without any back or sciatic pain.

3. Eighty-seven per cent of these patients were fully satisfied with the results of the operation.

4. The factors of age, trauma, or type of occupation appear to have no relationship to this type of injury. Also the type of operation appeared to be unrelated to the result.

5. Air myelograms while helpful were not as accurate as desired in our experience. Oil myelography, preferably with pantopaque as the contrast medicine, is the method of choice and should be routinely employed.

6. The end-results will be more gratifying in proportion to the degree of displacement of the nucleus pulposus.

7. Lost or diminished achillis reflexes do not often return, nor should a patient be allowed to believe paralyses will invariably recover following successful removal of the offending mass.

8. No relationship between increased narrowing of an intervertebral space and clinical result can be shown. Fusion of the vertebral bodies or dense bridging occurred in 6 patients, all of whom are in the group of clinically well. It could reasonably be postulated that more will develop this change as time goes on, but further follow-up studies will be necessary to substantiate or disprove this point.

9. It seems unlikely that the presence of a significant quantity of residual opaque oil in the caudal sac has any influence upon the clinical result.

10. The fundamental principle for good results is careful selection of patients with exclusion of those cases that fail to measure up to an exacting history and physical examination supported by myelography.

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THE MANAGEMENT OF KNEE INJURIES INCURRED IN COLLEGE FOOTBALL

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OF the various insults to which the body of a football player is subjected, injuries to the knee are among those fraught with the most serious consequences in terms of permanent disability. The middle-aged business man with a "trick knee" dating from his high school or college football days is commonplace. A considerable proportion of these injuries can be prevented or minimized by proper protective measures and prompt, adequate treatment.

The management of knee injuries has been a major concern of the medical staff of the Harvard Athletic Association since the appointment of the first team surgeon 58 years ago. The principles and policies which have evolved from this accumulated experience were first presented by Thorndike in 1938 (12). It is the purpose of the present report to review these principles and policies in the light of another decade of experience, and to present the results of their application during the 1947 season to the varsity, junior varsity, and freshman squads. The 174 men in this group constituted about one-third of the players regularly participating in contact sport during the fall season.

The management of any athletic injury is best considered from three points of view: prevention, immediate treatment and diagnosis, and definitive therapy.

PREVENTION

No player is allowed to don a uniform until a history of past illnesses and injuries has been taken and a thorough general physical examination carried out by a physician on the staff of the Department of Hygiene of the University. All old injuries discovered during this procedure are immediately reported to the medical department of the Athletic Association and are reviewed by the team surgeon concerned. Each knee is compared to the opposite knee with regard to quadriceps atrophy, lateral and medial collateral ligament laxity, cruciate ligament laxity, range of motion, and fluid (Fig. 1). Almost invariably roentgenograms are taken. Marked muscular weakness or instability disqualify the player for contact sport. He is instructed in quadriceps and hamstring strengthening exercises and advised to return a year later for re-examination. Those players who present minor degrees of ligament laxity, or a history of previous knee injury or operation are *strapped with adhesive tape before every practice session and game throughout the season.* The method of taping is known as the "Duke Simpson" strapping, after the trainer who first devised it, and provides, in effect, an extra set of collateral and cruciate ligaments outside the skin. Properly applied (Fig. 3), it produces great lateral and anterior-posterior stability with no appreciable interference in flexion or extension. It does not significantly decrease the player's speed. A varsity player wearing full equipment and with a Duke Simpson strapping on both knees was able to run 100 yards from a standing start in 11.8 seconds. Daily taping during a 12 week season is likely to produce skin irritation. Tincture of benzoin compound has been used in the past as a protection before each application of tape, but during the 1947 season, a formula devised by Dr. Martin Bellinger was found to be both cheaper and more effective:

Rosin G (powdered)	1 pound	(453.6 gm.)
Ethyl alcohol	1 gallon	(3785.4 c.c.)
Basic fuchsin	1 "pinch"	(0.15 gm.)

No candidate for the varsity, junior varsity, or freshman squads in 1947 was rejected because of weakness or instability of the knee. Of the 174 players comprising the squads, 31 required daily protective taping. Of these, 3 suffered a sprain of the medial collateral ligament during a game, and 1 a recurrence of a

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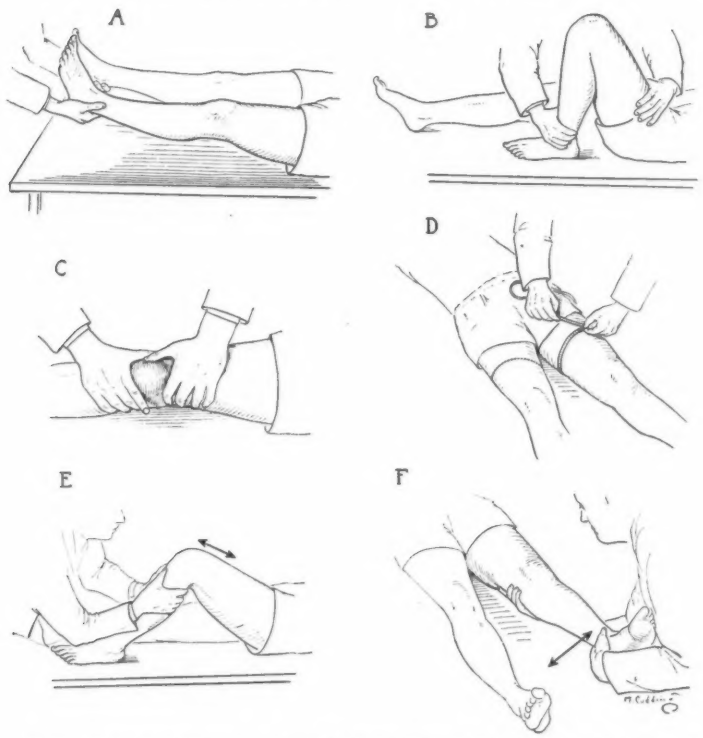

Fig. 1. Basic steps in examination of the knee: The subject is supine and completely relaxed. All steps are first carried out on the uninjured leg. A, Inspection and determination of extension. B, Determination of passive flexion. This follows a comparison of active flexion with the uninjured leg, and is not carried beyond the point of pain. C, Palpation for fluid. Pressure on the suprapatellar pouch drives small quantities of fluid downward. The right index finger is shown about to compress the anterolateral aspect of the joint, producing a fluid wave palpable by the thumbs and left hand. D, Determination of muscle atrophy. The circumference of the thighs is measured at the same level. E, Determination of cruciate ligament laxity. The knee is flexed at 90 degrees. The examiner's forearm presses firmly against the lower tibia while both hands grasp the leg just below the knee and manipulate it in the sagittal plane. F, Determination of collateral ligament laxity. One of the examiner's hands rests on the table and firmly grasps the femoral condyles. The other grasps the ankle and manipulates the extended knee in the coronal plane.

medial meniscus derangement. Occasionally in the past, the medial or lateral components of the taping have been torn during a practice session or game. This has not occurred since the practice of folding the long collateral strips of tape on themselves as they cross the knee has been followed (Fig. 3D).

IMMEDIATE TREATMENT AND DIAGNOSIS

The most important single factor in the management of knee injuries, or any other athletic trauma, is the presence of a qualified doctor on the playing field. To leave to a trainer the decision as to whether an injured player shall continue to play, or walk from the field, or be carried off, is to gamble with permanent disability with the cards stacked against the player.

Conservatism should be the team doctor's guiding principle. However partisan a "fan" he may be, he should remember that no final score is worth a permanent physical souvenir.

If, after examination on the practice or playing field, the doctor decides that further play is inadvisable, the player is taken, usually in a wheeled litter, to the field house where his clothes are removed and the knee carefully and gently surveyed for gross or major injury (Fig. 1). Except in obviously minor injuries, anteroposterior and lateral roentgenograms are taken. No exact diagnosis or prognosis is ventured at this time. If no major fracture is disclosed by x-ray examination and no obvious gross injury is present, a sponge rubber compression bandage is applied (Fig. 2); and the entire leg is immersed for 30 minutes in ice water. Ordinarily, this is accomplished within 10 minutes of the injury and is calculated to prevent hematoma formation at the site of the injury, whether it be a contusion, a tendon or ligament sprain, a derangement, or a combination injury. Sponge rubber known commercially as "tan open-cell sponge" is used and is compressed to half its thickness with elastic cotton bandage to produce a pressure of from 40 to 60 grams per square centimeter of skin. At the end of 30 minutes of chilling, the wet compression bandage is replaced with a dry one, the player is fitted with crutches, instructed in their use, and taken either to his room or to the infirmary to remain in bed until the next morning, with the leg supported on pillows above the level of the heart. The next afternoon, the bandage is removed, and again the knee is carefully surveyed. Any opinion given before this time is almost certain to be wrong. Twenty-four hours are required for enough localization of pain and tenderness to permit diagnostic manipulation. If the compression bandage has been properly applied, there will be little or no effusion. Occasionally there is slight edema of the leg distal to the bandage. Vascular complications, including thrombophlebitis, have not been encountered in any instance.

The injury is classified as a sprain, contusion, or meniscus injury; and appropriate definitive treatment is instituted.

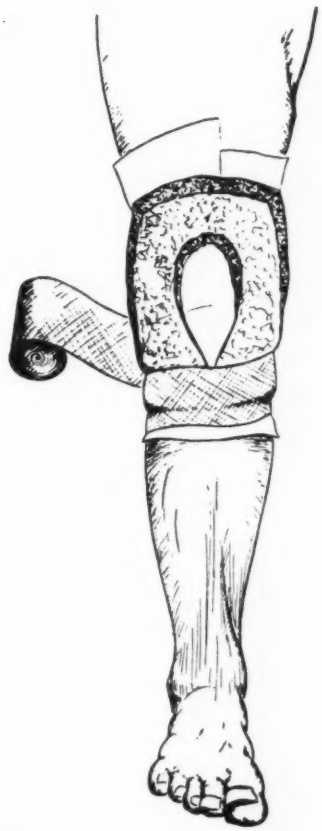

Fig. 2. Sponge rubber and elastic cotton compression bandage for immediate treatment of knee injuries.

DEFINITIVE TREATMENT

Contusions. Contusions are the least common and least serious of knee injuries. Daily definitive treatment consists of heat in the form of whirlpool baths, gentle stroking massage to stimulate lymphatic dissipation of hematoma, and active exercise. Sponge rubber compression bandages are reapplied after each treatment over the anterior aspect of the joint until the possibility of effusion has passed.

When function is normal, a padded fiber or plastic shield is taped over the site of the injury for a week or two lest a second blow at the same site produce a more disabling contusion. Nine contusions occurred during the season. Their severity and associated disability before the player could return to play are presented in Table I.

TABLE I.—CONTUSIONS OF THE KNEE

Grade of severity	1	2	3	4
Number of contusions	4	5	0	0
Days of disability	22	48	0	0
Average disability	5.5	9.6	0	0

TABLE II.—MEDIAL COLLATERAL LIGAMENT SPRAIN OF THE KNEE

Grade of severity	1	2	3	4
Number of sprains	2	11	0	0
Days of disability	16	166	0	0
Average disability	8	15.1	0	0

Grade 1 is the least degree of contusion which keeps a player from practice or play; grade 4 is the most severe compatible with conservative therapy. Contusions more severe than grade 3 are rare in football because of the protection afforded by standard equipment and the limitation of violent contact imposed by the game itself. Grade 3 and 4 contusions are much more common in skiing and automobile accidents.

Sprains. By far the most common knee injuries sustained in football are ligament sprains, and almost all are of the medial collateral (tibial collateral) ligament from external rotation and abduction of the tibia on the femur. The diagnosis is established by tenderness along the course of the ligament involved, by pain on tension of the ligament, and, in the severe grades, by demonstrable laxity. Treatment consists of crutches to rest the joint, compression to disseminate the hematoma produced by the partial rupture of the ligament, and to prevent synovial effusion, heat in the form of daily whirlpool baths, gentle massage, and active vigorous exercise against resistance without weight bearing as soon as it can be accomplished without pain. Splints or plaster casts have never been employed in the treatment of knee ligament sprains of less than grade 3 severity. The resulting atrophy of the vastus medialis muscle and, to a lesser extent, of the other quadriceps components and hamstrings prolongs the disability beyond the time required for healing of the ligament. Diathermy is never used in the treatment of any joint injury, since it very often produces effusion. Novocain has no place in the treatment of ligament sprains in athletes. It does not stimulate the proliferation of fibroblasts, and under its influence a minor sprain might easily become major. Every player who sustains a ligament sprain of any degree is protected thereafter at every practice session and game throughout his college career with a Duke Simpson adhesive tape strapping (Fig. 3). This practice follows the ancient axiom "once a sprain, always a sprain," and is based on the fact that the scar which unites the frayed or torn ligament is much less strong and resilient than the tissue it replaces.

Of the ligament sprains of the knee sustained in the 1947 season, only 6 were of the lateral (fibular) collateral ligament. Two minor cruciate ligament sprains occurred, but none in combination with, collateral ligament sprain.

The 13 sprains of the medial collateral ligament which occurred during the season are presented in Table II with regard to severity and the disability involved. Grade 1 is the least degree of sprain which can accurately be diagnosed. Grade 4 is complete rupture of the ligament.

Meniscus injuries. Undoubtedly, a number of the injuries described as sprains of the collateral ligaments were wholly or in part injuries to the menisci, of the type described by Smillie (10) involving the attachment of the ligament to the meniscus. However, these minor displacements in the young athlete almost always heal without disability on a conservative regimen and from a practical point of view are best considered as sprains.

The diagnosis of meniscus injury is not made without a history of an adequate rotation injury, locking, or "giving way," objective evidence of tenderness over the joint line, a positive "grinding" test (1) and, in posterior derangements, McMurray test (7) with normal roentgenograms. Osteochondritis dissecans is distinguished from meniscus derangement by roentgenograms and the characteristic locking and unlocking of the joint with little or no trauma or reaction.

Surgery is never carried out for a first meniscus injury unless irreducible locking is present, and then only after the associated sprain

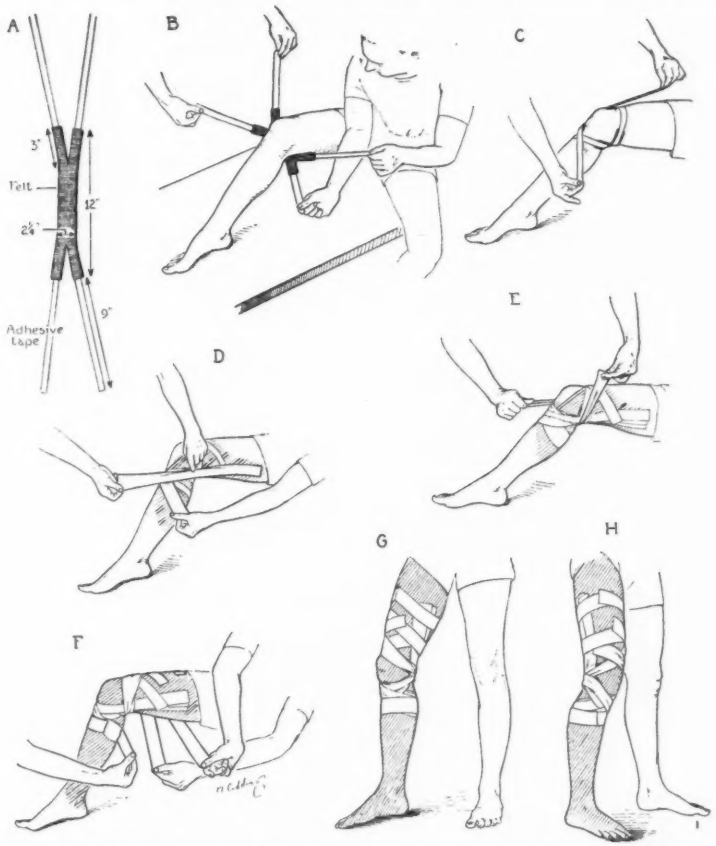

Fig. 3. The Duke Simpson protective knee taping. A, Details of the cruciate ligament supporting component. B and C, Application of the cruciate ligament supporting component. D, Application of medial and lateral collateral ligament components, three on each side. E, Reinforcement of cruciate ligament supporting component. Two strips of tape are applied, crossing anteriorly above and below the joint. F, Application of circular anchoring tapes. These are snug, but not constricting. G and H, The completed taping.

has been treated for 2 or 3 weeks and vigorous quadriceps exercise has been instituted. The usual management of meniscus injuries is well illustrated by the following case:

N. R., a 22 year old 210 pound varsity lineman, was struck by an opposing player on the lateral aspect of the left knee and complained of pain at the site of injury. He was removed from the game and the knee carefully surveyed. No abnormality was discovered, and since full speed running and "cutting" were possible without pain, he was returned to play. Several plays later, without further injury, the knee "gave way" and "something snapped" within it. Again he was removed from the game and again examination, including roentgenograms disclosed no abnormality. Cold and compression were applied and crutches were issued. Twenty-four hours later, there was slight effusion in the joint and fairly marked tenderness over the lateral collateral ligament from the joint line to the fibula. A diagnosis of sprain, grade 2, of the lateral collateral ligament was made; and definitive therapy consisting of wet heat, gentle massage, and guided exercise instituted. Recovery was slow, but 2 months later play was resumed with a protective strapping to the knee. On the first play after return to the line, the knee was moderately twisted and locked in about 45 degrees of flexion, with marked pain on its medial aspect. Once more,

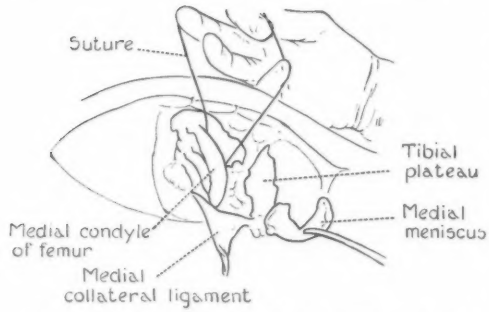

Fig. 4. Medial aspect of the knee at operation (Case 2). The joint is held in marked valgus. The medial collateral ligament has been withdrawn from the joint and the medial meniscus from the intercondylar notch. A suture has been inserted into the ends of the anterior cruciate ligament.

cold and compression were applied and crutches issued. Six days later, there remained a "rubbery" block to the last 30 degrees of passive extension, tenderness over the anteromedial aspect of the joint line, and moderate effusion. It was now obvious that the original injury had been, in all probability, an example of the occasional tendency of medial meniscus injuries to manifest themselves by symptoms referable to the lateral aspect of the joint. Vigorous quadriceps exercises were instituted; and 3 weeks later, a medial arthrotomy disclosed a "bucket-handle" laceration extending almost the whole length of the meniscus and displaced into the intercondylar notch. The lateral meniscus, as far as could be seen, was normal. The entire medial meniscus was removed. Quadriceps exercises were resumed immediately after operation, and 2 weeks later, crutches were discarded. Ten weeks after operation, protected by adhesive strapping, the player participated in spring practice except for scrimmages.

Only one other meniscus injury occurred among the squads under consideration during the 1947 season and this patient was not operated upon. It is unlikely that many meniscus injuries were overlooked since a close check is kept on the activities of all athletes throughout their college careers, and any disability of significance would soon appear. The 174 players in the group participated in 102 practice sessions and games during the season, resulting in approximately 17,000 exposures to injury. Since there were 2 meniscus injuries during the season, a player might be said to have an expectancy of injury to one or another of his medial menisci of 1:17,000. This low incidence is attributed to prevention and early treatment, and is in contrast to the experience of Simon (9) of Louisiana who found it necessary to remove 35 menisci from 33 football players in 4 years at one university.

Dislocations. The rarest, but by far the most serious football injury to the knee is luxation of the tibia on the femur. Although as a rule roentgenograms should be made of any dislocation before reduction, the extreme rarity of fractures about the knee in football players and the grave danger to which the nerves and blood vessels are exposed in dislocations make immediate reduction on the field in the few moments before muscle spasm and pain occur the procedure of choice.

One such case occurred during the 1947 season, the first in over 16 years:

V. M., a 24 year old, 200 pound back was struck on the lateral and posterior aspects of the left knee by the flank of an opposing player. The foot remained fixed; the partially flexed knee was forced into extreme valgus and the femur was rotated internally approximately 90 degrees. The patella was dislocated laterally. Peripheral pulses and motion of the toes and ankle were normal. Within 1 minute of the injury on the field, reduction was easily effected with almost no discomfort or difficulty. Roentgenograms disclosed no evidence of fracture. A sponge rubber compression bandage was applied and a temporary plaster of paris cylinder from the toes to the groin with the ankle at 90 degrees and the knee in 30 degrees of flexion. Four days later, the joint was exposed through a long curved medial incision (Fig. 4). The medial collateral ligament was found to be avulsed from its tibial insertion and lying within the joint, its distal end in the intercondylar notch. Both cruciate ligaments were ruptured near their insertions. The medial meniscus was displaced to a vertical position in the intercondylar notch. The meniscus was removed, the torn ends of the cruciate ligaments approximated, and the distal end of the avulsed lateral collateral sutured in place. Fine interrupted cotton sutures were used throughout. Quadriceps exercises were begun immediately after operation and active motion on the eighth postoperative day. Crutches were discarded 2 weeks later. Three months after operation, there was slight cruciate laxity, 10 degrees of lateral laxity, a normal active and passive range of motion, and the circumference of the left thigh was 1 inch less than the right. The player participated in winter track and spring baseball.

Although authoritative American and European opinion in general frowns upon operative intervention (2,5,10,11,14) prolonged immobilization would have accomplished little in this

TABLE III.—INCIDENCE OF ALL KNEE INJURIES WITH REGARD TO POSITION PLAYED

Position	Backs (4)	Ends (2)	Linesmen (5)
Average number of exposures per injury	246	299	208
Average disability in days per injury	13.2	11.8	17.2

case, with the entire medial meniscus displaced into the intercondylar notch and the avulsed medial collateral ligament lying between the tibia and femur. Examination (Fig.1) under anesthesia followed by whatever surgical exposure is indicated (8), carries little risk, establishes the diagnosis with precision, and may well make a great deal of difference in subsequent disability. Fortunately, no injury to the popliteal artery occurred in this case. When ischemia of the leg is apparent after reduction of a dislocated knee, immediate surgery is indicated. As soon as possible, the popliteal space should be explored, the damaged segment of artery inspected and, if necessary, excised or replaced with a vein graft, a lumbar sympathectomy carried out, and heparinization instituted. The experience of the two world wars with regard to wounds of the popliteal artery is disheartening (3, 4, 6, 13), and only by such vigorous measures can gangrene be averted.

Statistical analysis with regard to position played. It is of interest to study the incidence of knee injuries in general with reference to the position of the injured player on the team. The data are presented in Table III.

SUMMARY

1. The principles and policies of the medical department of the Harvard Athletic Association with regard to the management of knee injuries sustained in college football are presented.

2. Prevention, immediate treatment, and definitive therapy of contusions, sprains, meniscus injuries, and dislocations are discussed.

3. The results of treatment of knee injuries occurring in the varsity, junior varsity, and freshman squads during the 1947 season are presented.

4. Two illustrative cases are presented.

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THE EVALUATION OF SULFATHALIDINE AND STREPTOMYCIN AS ADJUNCTS IN PREPARING THE LARGE BOWEL FOR SURGERY

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THE value of antibacterial agents in preparing the bowel for surgery is recognized by the majority of surgeons and widely acclaimed by many as the greatest recent advancement in this field. A few surgeons have achieved excellent results without the use of these agents; nevertheless, it is our opinion that succinylsulfathiazole (sulfasuxidine) and phthalysulfathiazole (sulfathalidine) have been influential factors in the relatively recent reduction in the mortality attendant upon surgery of the colon and rectum. The latter is exemplified by a recent series, performed by one of us (H. E. B.) of 146 consecutive bowel resections without a fatality.

Regardless of the merit of these drugs, even the skeptic must admit that it would be ideal to have the bowel lumen aseptic at the time surgery is performed. Realizing that more potent antibacterial agents should be advantageous in further reducing the bacterial flora of the colon, our interest was aroused by reports of various workers relative to the effect of oral streptomycin in experimental animals (3, 5, 11, 12). Since this substance was found to be effective against gram-negative bacilli (4, 5, 10), was absorbed very poorly from the intestinal tract (12, 13), and, therefore, relatively nontoxic systemically, the thought immediately arose that here might be another useful adjunct in preparing the large bowel for surgery. It seemed likely that a combination of streptomycin and sulfathalidine might be even more efficacious chemoprophylactically. A clinical and bacteriological evaluation of streptomycin, as well as a combination of this substance with the sulfonamides, was therefore deemed advisable.

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TECHNICAL RÉSUMÉ OF THE STUDY

At the time of conception of this study, no reports were found in the literature relative to the effect of oral streptomycin on the bacterial flora of the large bowel in human beings. Due to the presence of such factors as partial obstruction, secondary infection, and lowered resistance, which are found in the presence of carcinoma of the bowel, it was felt that the use of patients who were actually being prepared for operation would enhance the value of the results. This made the problem more difficult, prolonged its termination, and necessarily curtailed the number of patients studied. However, all of the latter had carcinoma of the colon or rectum, with one exception.

An attempt was made to control some of the variable factors which might influence the bacterial flora. After admission to the hospital, patients were fed a general diet until two preliminary stool specimens were obtained. After the second preliminary stool specimen was secured, the drug was administered and all subsequent stool specimens were collected and numbered, labeled according to the time of passage, date, hour of administration and type of drug. They were stored in a refrigerator immediately to prevent further bacterial growth. Each patient was placed on the same high caloric, high protein, nonresidue diet supplemented by protein carbohydrate mixtures (2800 to 3000 calories daily). A fluid intake of 2500 to 3000 cubic centimeters daily was maintained. Only one dose of laxative was given to each patient 36 hours prior to operation. Patients requiring barium or cleansing enemas were eliminated. Individual studies usually ex-

tended over a 6 or 7 day period but varied in a few cases from 2 to 12 days.

Previously, a brief comparative study of the relative effects of sulfathalidine and sulfasuxidine on the fecal coliform bacterial counts was made by three of the authors. The results were not sufficiently standardized to be included in the present study. Consequently, sulfathalidine, 0.1 gram per kilogram of body weight, was administered daily in 6 doses to the first group of patients. The second group of patients received streptomycin, 2 grams daily, dissolved in 12 cubic centimeters of water and administered in 2 cubic centimeter doses every 4 hours with a small amount of water. Several patients received a combination of streptomycin (2 gm. daily) and sulfathalidine (0.1 gm. per kgm. of body weight daily).

BACTERIOLOGICAL STUDIES

A complete bacteriologic procedure for evaluating intestinal antiseptics must necessarily consider all types of bacteria found in the gastrointestinal tract. The entire flora of man is extremely varied and, to name only a few of the most important groups, consists of coliform bacilli (Escherichia coli, Aerobacter aerogenes and related organisms), enterococci, Clostridia, Bacteroides and the Shigella group of bacillary dysentery. Obviously, the task of isolating and accurately identifying so many diverse species is an extremely complex one which the authors were not prepared to undertake. Instead, two simpler methods were adopted, namely, (1) coliform count and (2) "total count." In the first named procedure a series of dilution tubes are cultured on eosin methylene blue agar, the coliform colonies counted, and this figure used to estimate the number of organisms in the specimen. The latter term, "total count," denotes a method whereby an attempt is made to culture and count all of the important aerobes and anaerobes. Appropriate dilutions are added in duplicate to sets of veal infusion agar plates, one incubated aerobically, the other anaerobically. The word "total" is used with qualification since the medium employed does not permit growth of certain bacterial genera, notably, the lactobacilli.

Neutralization of drugs. The relatively large amounts of sulfathalidine present in the specimens could be effectively neutralized by incorporating 5 milligrams per cent para aminobenzoic acid in the water dilution tubes. Satisfactory inactivation of streptomycin was obtained with semicarbazide (8). The procedure was modified from that described by Rake and Donovick in that sodium acetate was employed in place of the potassium salt. From preliminary trials it was determined that effective inactivation occurred within 5 minutes and that the concentration of semicarbazide-acetate carried over to culture plates was not itself inhibitory. Since high concentrations of streptomycin could be expected to be present in specimens, it was necessary to determine how much could be inactivated under the test conditions. This figure was found to be 1320 micrograms per cubic centimeters which is the amount present in the first dilution tube from a 132 milligrams per gram specimen. The amount of streptomycin present in the feces of patients receiving 2 grams per day was determined by examining 80 random specimens and found to vary from 240 to 12,000 micrograms (12 mgm.) per gram. Thus, the method appears to provide for more than tenfold the highest concentration actually observed.

Drug susceptibility. As the study progressed the problem of reversion became more eminent and an explanation of the basis for this phenomenon was sought as well as proof that organisms actually were developing resistance to streptomycin. Consequently at the time of isolation, selected strains were subcultured and stored in the refrigerator until needed. Susceptibility to streptomycin was estimated by the method of Bondi and associates. Sulfathalidine susceptibility was determined by the conventional broth tube dilution procedure.

Thirty-one isolations from 13 patients were studied in some detail for drug susceptibility. In each instance a coliform organism from a preliminary specimen was compared with one or more strains isolated during administration of drug. These bacteriological studies are being reported in detail in a separate publication.

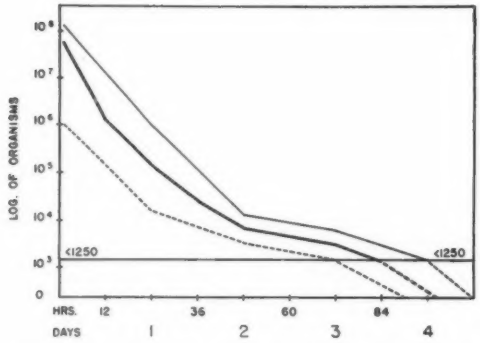

Chart 1. Coliform counts after sulfathalidine administration, 0.1 gram per kilogram of body weight, daily. ———, Highest count in any patient; ———, average count in 6 patients; — — —, lowest count in any patient.

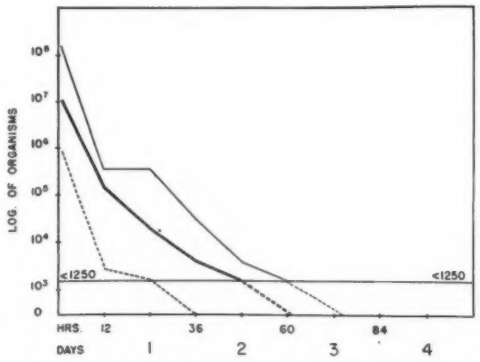

Chart 2. Coliform counts after streptomycin administration, 2 grams daily. ———, Highest count in any patient; ———, average count in 9 patients; — — —, lowest count in any patient.

RESULTS

Sulfathalidine. Seven patients, all with adenocarcinoma of the rectum, were given sulfathalidine. The results were uniform in 6 patients and are depicted in Chart 1. The preliminary counts varied from 10^6 to 10^8 and within 3 to 4 days dropped to less than 1250 organisms per gram of wet feces. The average drop occurred in 3½ days. Many of the plates at this time had no growth at all; but since the use of lower dilutions was not considered practical, values less than 1250 organisms per gram of wet feces were not determined. When the coliform flora has been decreased from 10^7 to 1000 it represents a reduction of 99.99 per cent.

One patient failed to respond in the usual manner. The explanation for this failure is not obvious since medication, diet, etc., were properly administered and the patient was very co-operative. Yet, the count remained high for 7 days and at the end of 10 days was still 12,500 organisms per gram of wet feces.

Streptomycin. When this study was conceived, there was some question concerning the quantity of streptomycin that should be used. After conferring with Dr. J. Carlisle, 2 grams was selected as the daily dosage. This was dissolved in 12 cubic centimeters of water and administered orally in 6 doses, 2 cubic centimeters every 4 hours, followed by a glass of water. Twelve patients received 2 grams of streptomycin daily. One patient had a recurrent carcinoma with a rectovesical fistula following sigmoidectomy performed at another hospital. At the end of 4 days his counts remained exceedingly high. In 2 other patients somewhat bizarre results were obtained. In 1 patient a susceptible Aerobacter aerogenes was isolated from the preliminary specimen, and at the end of 62 hours a very resistant coliform organism (unidentified) was isolated from a stool with a 9,000,000 coliform count. In the other patient a susceptible coliform organism was isolated from the preliminary stool. At the end of 33 hours the coliform count in this patient was 260,000,000, and a resistant Escherichia coli was isolated. Operative intervention prevented further study, and it was felt that definite conclusions should not be drawn in these instances.

Chart 2 diagrammatically represents the rather spectacular results which followed the oral administration of streptomycin in the 9 remaining patients. It was interesting to note that in 2 patients the count approached less than 1250 organisms within 12 hours. The longest time required for a drop to less than 1250 was 60 hours; while the average time required was 48 hours.

Results were so excellent in the majority of these patients that it appeared that some of the streptomycin might have been wasted. Consequently, a daily dose of 0.5 gram was employed in 6 patients. The results were in-

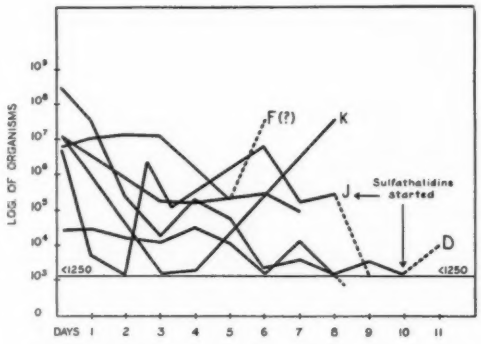

Chart 3. Coliform counts after 0.5 gram streptomycin daily. Reversion in 2 patients (K and J).

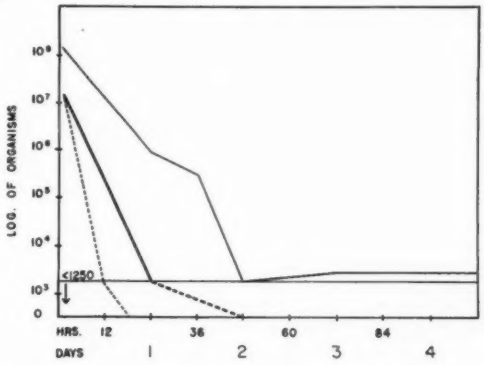

Chart 4. Coliform counts after combination of streptomycin, 2 grams daily, and sulfathalidine, 0.1 gram per kilogram of body weight, daily. ———, Highest count in any patient; ———, average count in 11 patients; — — —, lowest count in any patient.

consistent (Chart 3) and in general the counts decreased slowly in this group. Reversion apparently occurred in patient K (Chart 3), and probably in patient J. In the latter patient sulfathalidine was started on the 8th day, and the count was less than 1250 organisms within 24 hours. Reversion apparently occurred in patient F also. The elevation of the final count in patient D to 10,000 organisms per gram of wet feces may or may not be significant. From these observations it was obvious that 0.5 gram of streptomycin was not the optimum dosage.

Combined administration. Fourteen patients received combined therapy. It was necessary to eliminate 2 patients who received the correct dosage of sulfonamides but only 1 gram of streptomycin. Twelve patients received 2 grams of streptomycin and 0.1 gram of sulfathalidine per kilogram of body weight daily. A preliminary report of this work was given recently (1) and with the exception of minor changes our results and conclusions are the same at the present time. Results were exceptionally uniform during the first 3 days (similar to streptomycin above). In all patients, except one, the coliform counts were less than 1250 organisms per gram of wet feces within 48 hours. In the exceptional patient (patient B in Chart 5) the counts remained exceedingly high for 5 days and, had these counts been included in the results which are shown in Chart 4, the average would have been completely distorted.

In most of these patients studies were carried on for several days, and reversion of the counts was encountered in 3 patients. A graphic representation of this phenomenon may be seen in Chart 5. In each instance resistant organisms were isolated after the counts had returned to levels of 10^4, 10^6, and 10^8.

Total fecal bacterial counts. The desirability of studying the entire fecal flora was recognized from the beginning of this problem. Because of the extensive work required for such studies, however, it was decided to use coliform counts for the most part. Both coliform and total counts were performed on all specimens from 6 patients receiving a combination of sulfathalidine and streptomycin.

In 5 instances the coliform count dropped promptly and no reversion was noted; the sixth patient showed a slow, gradual decrease for 5 days and reversion at 10 days. No significant change in total count was noticed in 2 instances, and only a partial, temporary drop in the other four. Streptomycin-resistant organisms were isolated from the late specimens of all 6 patients.

DISCUSSION OF RESULTS

In the beginning of this study the authors believed that evaluation of streptomycin and sulfathalidine as chemoprophylactic agents would not be too complex, but as our obser-

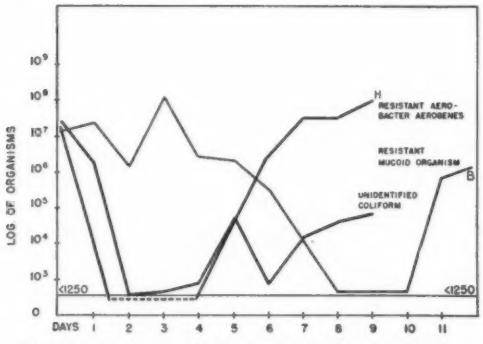

Chart 5. Reversion. Coliform counts following combination of sulfonamides and streptomycin, 3 of 12 patients.

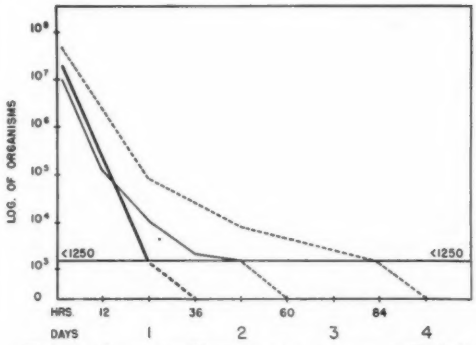

Chart 6. Average coliform counts. — — —, Sulfathalidine, 0.1 gram per kilogram of body weight daily; ———, streptomycin, 2 grams daily; ———, combined, same dosage.

vations progressed the use of several patients was precluded by complicating factors such as incorrect diet, inadequate medication, and improper collection of specimens. In any case where there was some doubt as to the validity of the results, the patient was eliminated. In complying with these requirements the total number of patients included in evaluating the results was reduced to 33.

Although this series is not large, certain conclusions of clinical and bacteriologic value may be conjectured.

The results with sulfathalidine served merely to verify the work of Poth (6). There were only 7 patients in this group, but the results were very consistent in 6. The bacterial counts dropped in every patient to a satisfactory level prior to surgery, although the average time required was 3½ days. No obvious reversion occurred in this group. One may conclude that sulfathalidine is a reliable agent for decreasing the coliform bacterial flora of the large bowel prior to surgery.

From our observations, large doses of streptomycin (2 gm. daily) appear to be excellent for reducing certain strains of coliform organisms in the large bowel, and other investigators (14) have found it to be effective in reducing clostridal organisms. It was obvious from the results obtained after the administration of 0.5 gram of streptomycin daily that this dosage was not adequate. The reversion that occurred in patients K and J (Chart 3) was due to the appearance of a streptomycin-resistant coliform organism. The frequent occurrence of this phenomenon would apparently preclude the use of such small doses of streptomycin.

Results in the group of patients who receive a combination of streptomycin and sulfathalidine were somewhat disappointing, since it was our hope that sulfathalidine and streptomycin in combination would entirely prevent reversions due to the appearance of drug fast organisms. Such was not the case. However, the combination of drugs was superior to either one alone in one important respect, namely, the rapidity with which the coliform count dropped (see Chart 6). If the study of these patients had been limited to 3 days the results would have been classified as excellent. Fortunately, most of the studies were extended over longer periods of time and other important observations were made, for example, the frequency with which reversion in counts occurred. Although it is well known that drug-resistant organisms often appear during treatment with streptomycin, we had hoped that combined administration with sulfathalidine would prevent the occurrence of this phenomenon. Nevertheless, 3 of the 12 patients had a reversion of their counts and pure cultures of streptomycin-resistant organisms were isolated in each instance. One was apparently resistant to sulfathalidine, but the others were not tested. In patient H contamination occurred during the operation with a resulting peritonitis, multiple intra-abdominal abscesses, and death. Without the aid of the antibiotics and sulfonamides, therapy was hopeless. The re-

covery of streptomycin-resistant organisms from the late specimens of the 6 patients in this group, upon whom total counts were performed, adds further support to the theory, that prolonged administration of streptomycin is not desirable. It is unlikely that a combination of these drugs, at least in the doses used by us can significantly alter the total bacterial population for prolonged periods of time.

Analysis of the bacteriologic data suggests only one explanation for the reversion in coliform counts which were encountered; i.e., the appearance and multiplication of a drug-resistant organism. On the other hand, reversion did not always accompany the appearance of a resistant coliform, provided the patient was receiving both streptomycin and sulfathalidine. The obvious explanation for such a discrepancy is that those bacteria resistant to streptomycin were, nevertheless, susceptible to the sulfonamide. Experimental evidence to support this view was obtained in several instances. Thus, the development of resistant coliform organisms should occur less frequently in patients receiving a combination of the two drugs. Although our data show reversion occurring as frequently in the group receiving the combination as in the group with streptomycin alone, this is possibly due to the limited number of cases involved.

The results obtained with the combination of drugs indicate that administration for 24 hours is sufficient to reduce the coliform population of the bowel by approximately 99.99 per cent. Apparently no harm is done by continuing the program for a total of 48 hours. Further prolongation, however, runs the risk of encouraging development of bacteria resistant to streptomycin and should be avoided.

Although we found that sulfathalidine required on the average 3½ days to produce a base-line drop in coliforms, Poth's figures in a large series of cases indicate that 5 to 7 days may be necessary for consistent results. Because he has obtained such excellent healing of intestinal anastomoses with this regimen (6), we hesitate to recommend a shorter period. Since combined administration appears to have merit, we feel safe in proposing the use of sulfonamides for 5 days with the addition of streptomycin 48 hours prior to surgery.

It should be emphasized that the chemoprophylactic program recommended was not subjected to bacteriological study, but, rather, is derived from our results. In the future it may be found that larger doses of streptomycin are advantageous.

In these preliminary experiments we have limited ourselves largely to the coliform count. Escherichia coli is only one of the many intestinal inhabitants. Recent studies by other investigators, as well as our own limited data obtained from "total counts," indicate that fecal coliform counts do not accurately reflect trends in total population. More accurate evaluation of the chemoprophylactic effectiveness of the sulfonamides and streptomycin must await results of more detailed studies.

SUMMARY

1. Certain properties of streptomycin indicated that it would be a valuable adjunct in preparing the large bowel for surgery. Therefore, a comparative evaluation of sulfathalidine, streptomycin, and combinations of the two was undertaken, patients with carcinoma of the rectum or colon being used as subjects.

2. The intestinal bacterial flora was studied by means of coliform and total bacterial counts. An explanation of reversion of these counts was sought through the study of drug susceptibilities of selected strains of organisms.

3. The average fecal coliform count decreased by 99.99 per cent in 3½ days with 0.1 gram per kilogram of body weight daily of sulfathalidine, in 2 days with 2 grams of streptomycin, and in 24 hours with a combination of the two.

4. Reversion in count due to resistant organisms was not observed with the sulfonamide, but did occur with streptomycin, especially in those patients who received (0.5 gm.) daily. Combined use of the two drugs did not entirely prevent this phenomenon.

5. A coliform organism which became resistant to both drugs preoperatively, was responsible postoperatively for a generalized peritonitis which proved fatal.

6. On the basis of our preliminary experiments the use of streptomycin alone cannot be recommended. However, a program which includes sulfathalidine for 5 to 7 days and the addition of streptomycin 48 hours prior to sur-

gery is worthy of trial. With this program, the benefit of the higher antibacterial activity of streptomycin is obtained, and the risk of producing resistant organisms is thus minimized.

7. Bacteriological studies indicated that the coliform count fails to reflect accurately the total colonic bacterial population including important pathogenes.

8. More conclusive evaluation of the effectiveness of these drugs on the fecal bacterial flora awaits the results of similar and more detailed investigation.

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TUMORS OF THE VERTEBRAL COLUMN

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ABNORMALITIES in the density, structure, or general configuration of the vertebral bodies or neural arches may be produced either by tumors arising primarily in the vertebral column or surrounding structures or as a consequence of metastasis from neoplasms located in other parts of the body. Due to the proximity of some important organs and of the central nervous system to the vertebral column, the prognosis as well as the treatment of these tumors is somewhat different from that for the same type of lesions located in the extremities. In order to obtain a better clinical understanding of these neoplasms, we studied all the patients with tumors of the vertebral column seen at the State University of Iowa Hospitals with good clinical and roentgenographical follow-up.

It is not our aim to discuss all the aspects of this problem or to give a complete review of the literature but to describe in detail those vertebral tumors, which, due to their localization, evolution, response to treatment or end-result, warrant consideration. Although this report is mainly concerned with the primary tumors of the vertebral column, tumors affecting the spine through contiguity or metastasis were also included. Only the primary tumors of the vertebral column which could be examined microscopically and the metastatic tumors to the spine with known primary lesion were included in this study.

HEMANGIOMA

Two patients with hemangioma of the vertebra were studied. One of these tumors was found at autopsy in the body of the eighth dorsal vertebra. It had never produced clinical symptoms.

The second patient was a 42 year old woman who sustained a fall 6 months prior to admission. Then she complained of numbness in both legs and right arm, and difficulty in walking. Neurological examination showed the presence of compression of the spinal cord at the level of the lower cervical spine. The anteroposterior roentgenogram showed a honeycomb-appearing lesion involving the body and neural arches of the seventh cervical vertebra. The lateral roentgenogram showed a marked increase in size of the vertebral body, bulging of the walls, and new bone formation (Figs. 1a and 1b).

The patient was treated by means of roentgen therapy, with temporary improvement of the symptoms. However, the patient's condition became suddenly worse, and an almost complete paralysis on the right side of the body developed. A laminectomy was immediately performed and on removal of the lamina of the seventh cervical vertebra, the bone was found to be very vascular. No extradural soft tissue tumor was encountered. Microscopical studies confirmed the diagnosis of hemangioma. The patient recovered very quickly following the operation, and when last seen in this hospital, 13 months after operation, the only residual symptom was a slight weakness of the right arm. The roentgenogram at that time showed the lesion to be unchanged.

While vertebral hemangiomas are frequently found at autopsy (10.7% in Schmorl statistics; 11.93% in Topper statistics), the diagnosis is rarely made clinically. This may be due either to the lack of symptoms given by the vertebral hemangiomas, or to the difficulty of its roentgenographic visualization. Connell and Hay, and Hammes have reported proved cases of hemangioma involving the neural arches in which repeated x-ray examinations were completely negative.

The usual site of the vertebral hemangioma is in the dorsal and lumbar regions (Blackford, Kelly, Perman, Livingston, Ireland). Hemangioma of the cervical vertebrae is an extremely rare entity. Bucy and Capp in 1930 stated that there were no cases involving the cervical vertebrae. Heaney and Whitaker reported in 1933 the first case involving the axis, but their diagnosis was based on the roentgenogram only and no histological examination was obtained. The first histologically proved case of hemangioma involving the cervical spine and producing compression of the spinal cord, was reported by Geschickter and Keasbey. It involved the bodies of the fourth, fifth, and sixth cervical vertebrae.

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Schlezinger and Ungar in 1939 described another histologically proved case, involving the seventh cervical and causing compression myelopathy. In 1941, Ghormley and Adson reported 39 cases of vertebral hemangioma, of which only 1 was of cervical localization.

Holta in 1942 reported a new proved case involving the body of the fourth cervical that had produced a pathological fracture.

Due to the fact that many of the present day foreign periodicals are not available, a complete review of the literature was impossible. However, investigation of most of the American and foreign publications since 1930 has failed to reveal any additional cases. Consequently, our patient may be considered the sixth case of cervical hemangioma producing clinical symptoms, to be reported in the literature and the fourth one of such localization proved by microscopical studies.

Regarding the treatment of this condition most authors agree that the best results can be obtained by means of roentgen therapy. Surgical intervention is advisable when there are persistent signs of cord compression, but otherwise is contraindicated because of the high mortality produced by the postoperative bleeding (1 of 5 patients operated upon according to Ferber and Lampe; 21.1% mortality according to Schlezinger and Ungar).

The increase of the neurological signs following roentgen therapy in our patient, justified surgical intervention.

GIANT CELL TUMOR

Since 1924, when Lewis reviewed 16 cases previously reported in the literature and added a new one, several authors have described this condition (Santos and Jenkinson and Hunter, McFarlane and Linell, Willard and Nicholson), making a total of 91 cases reported up to 1945 (Brock and Bogart).

In the files of this hospital, 2 cases of giant cell tumor involving the spine were found. Both were in patients of the same age and the lesions were localized in the second and third sacral segments. Although according to Richards and Singleton, giant cell tumors of the spine may be of the osteolytic or of the osteoblastic variety, both our patients had a purely osteolytic lesion involving one sacral segment.

Both lesions appeared in patients belonging to the same age group and in the same location; however the end-results were completely different:

A 13 year old male was seen here 4 months following direct trauma over the sacrum. He complained of localized sacral pain present only when sitting. His general condition remained excellent throughout. On local physical examination a tender spot 2 inches below the posterosuperior iliac spine was found. On rectal examination, a tumor situated in front of the sacrum was palpable. Roentgenographic studies demonstrated the presence of an osteolytic lesion that had entirely destroyed the third sacral segment (Fig. 2a). No periosteal reaction was present. A biopsy was performed and during operation the destruction was found to have been so complete that a finger could be introduced through both walls of the sacrum. The frozen sections demonstrated a giant cell tumor, and it was decided to suture without any further surgery.

The patient received 800 roentgens postoperatively. Serial roentgenograms taken every few months demonstrated disappearance of the osteolytic area and reconstruction of the second sacral segment (Fig. 2b). There was no metastasis.

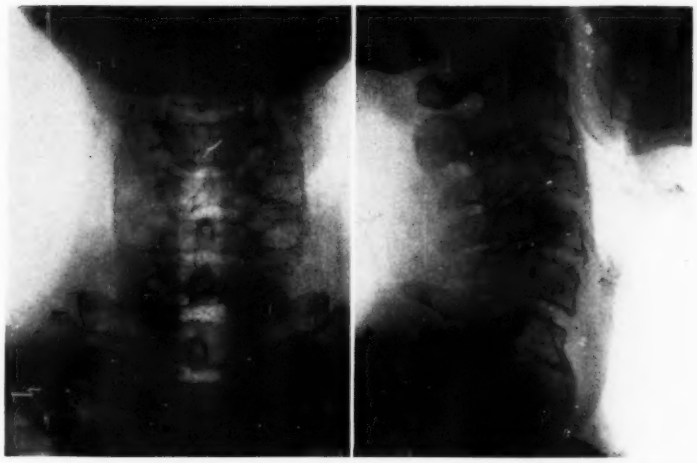
The patient was periodically checked for at least 3 years. Six years after biopsy, the patient was in excellent general condition and in active military duty.

The other patient, a 13 year old female had spontaneous onset of paresthesias in both legs without previous trauma. One week later, bladder disturbances and weakness of the lowers were present. On admission (3 weeks after the onset of symptoms) her gait was unsteady and her legs very weak. Physical examination demonstrated the existence of anesthesia over the second, third, and fourth sacral dermatomes, loss of rectal tone and absent deep reflexes in the lowers. Spinal fluid and blood chemistry studies were negative. Complete destruction of the second sacral segment was observed in the roentgenograms.

A very vascular tumor growing around the sacral roots and completely destroying the second sacral segment was found at the operation. Due to the infiltrative character of the process, only a partial removal of the mass was possible. Following surgery 1200 roentgens were given.

The patient progressively improved and a few weeks afterward she was able to walk, the rectal and bladder control being again normal.

Two months after operation, patient developed a sudden catch in the left side of her back. Most of the previous signs recurred, this time being more marked on the left lower extremity. Physical examination showed the presence of a fluctuant swelling about the size of an apple, over the sacral region. Aspiration biopsy confirmed the recurrence of the giant cell tumor, but no histological signs of malignancy were found. The roentgenograms showed



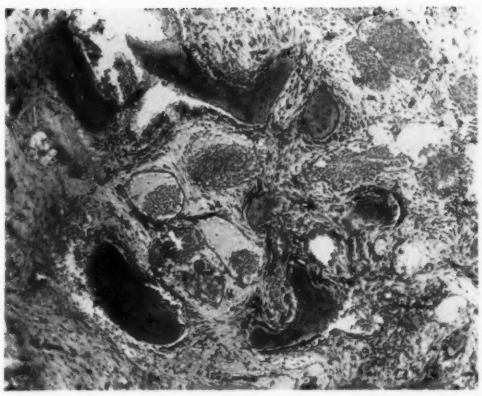
a b

Fig. 1. a and b, Hemangioma involving the seventh cervical vertebra. c, Microscopic aspect, low power.

advanced destruction of the sacrum and a pathological fracture through the wing of the sacrum was already present. Further roentgen therapy was administered. The patient died 16 months after the initial surgical intervention.

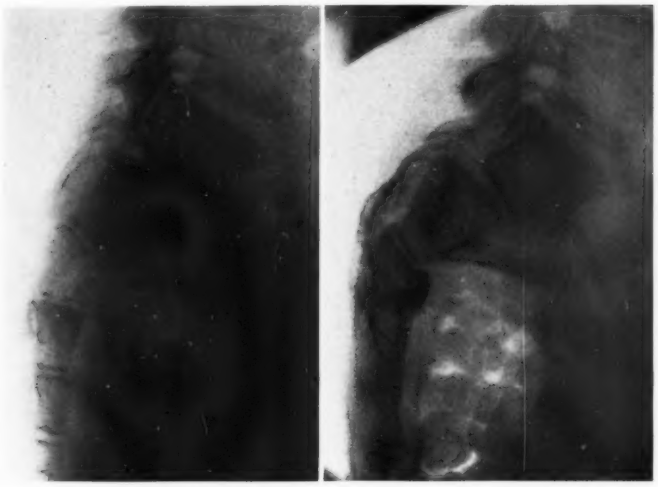
The end-results obtained in these two giant cell tumors which were devoid of pathological signs of malignancy were striking. Although both patients were operated upon, in the first one only a biopsy was performed. In the second case a partial removal was necessary due to presence of neurological signs of compression. Some authors state that biopsy (Brailsford, Kolodny, and Pfahler and Parry), curettage, partial or total removal (Bower, Clark and Davis) may stimulate further activity or facilitate the apparition of recurrences, especially when they are combined with irradiation (Coley and Higinbotham). As in our second case patient was treated by means of partial removal plus x-ray therapy, it is possible that the treatment influenced the evolution of the tumor, but it will be unfair to forget that the partial surgical removal was not an elective measure, but determined by the intrinsic infiltrating characteristics of the tumor—characteristics that were not present in the first case.

On establishing the indications for the treatment of giant cell tumors of the spine, we must



c

take into consideration their location. When they involve only the neural arches, successful cures after complete removal have been reported (Vegh, Milch). If the involvement of the vertebral body is only partial and in an area close to the pedicles, successful results can also be obtained by removal of the involved arches and curettage of the vertebral body (Duncan and Ferguson). When the tumor occupies most of a vertebral body, the treatment of choice is roentgen therapy. Several cases have been described in the literature in which a complete reossification of the vertebral body took place following treatment, as



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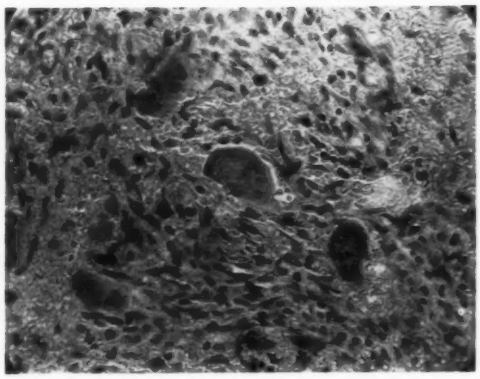

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Fig. 2. a, Destruction of the body of the third sacral segment 4 months after onset. b, Reconstruction of the third sacral segment following x-ray therapy. c, Microscopic aspect, high power.

happened in our first case (Brock and Bogart, Brunschwig, Cotton).

Spontaneous cures may occur, as described in a case reported by Murphy following pathological fracture.

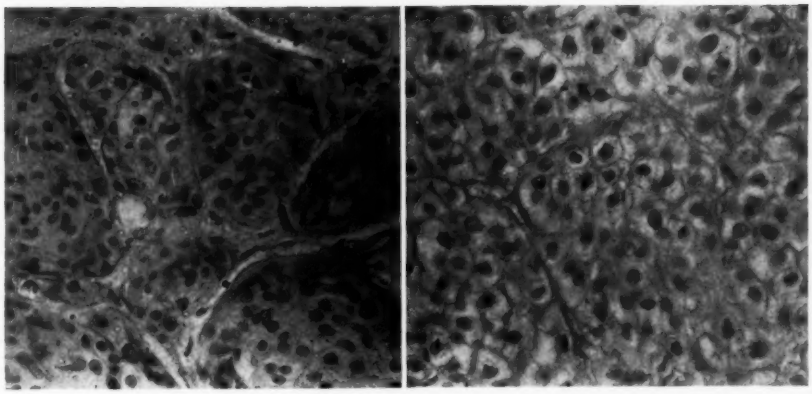
CHORDOMA

According to Ehrenhaft notochordal tissue remnants are found during postmortem examinations in 2 per cent of the cases. They usually appear in those areas in which only a moderate amount of cartilaginous tissue surrounds the chorda, i.e., the base of the skull and sacrococcygeal region. However, they may appear at any level of the spine and undergo malignant degeneration, giving origin to tumoral neoformations.

The clinical signs of these tumors depend, to a great extent, on their location. The roentgenograms usually show an area of rarefaction without signs of new bone formation. In the advanced stages, a soft tissue shadow can also be observed.

The microscopical structure of the chondromas is by no means uniform. Regional variations can be observed even in the same tumor. Among our material, there was a specimen (for which a clinical record was not available but that was included in this report because it allowed an excellent histological understanding of this condition) in which some regions appeared formed by solid rods of cells having an epithelial appearance (Fig. 3b). In other regions the tumoral cells had a clearer protoplasm or presented a marked distended protoplasm full of mucinous material (physaliphorous cells of Virchow).

The process of vacuolation and mucin formation is more pronounced in other cases in



b c

Fig. 3. a, Chordoma destroying the sacrum. Photograph obtained from a microscopic slide, enlarged 2 times. b, Microscopic aspect through the upper part of the tumor. High power. c, Microscopic aspect through the lower part of the tumor. High power.

which the cells adopt a syncytium-like appearance. A great amount of mucin is present in the intercellular spaces (Fig. 4b). Areas of necrosis are not infrequent.

These different histological aspects have been explained by Alezais and Peyron on basis of the different stages of evolution of the notochord. Steward described the presence of nuclear vacuolation, and stated that it was more frequent in the cellular parts of the tumor, being apparently absent in the areas with abundant mucin. Steward and Morin reported the existence in these tumors of spherical bodies formed by concentrically arranged groups of cells that they compared to "nests of beakers." Although the presence of such formations has been confirmed by Cappell, we were unable to find them in our histological sections.

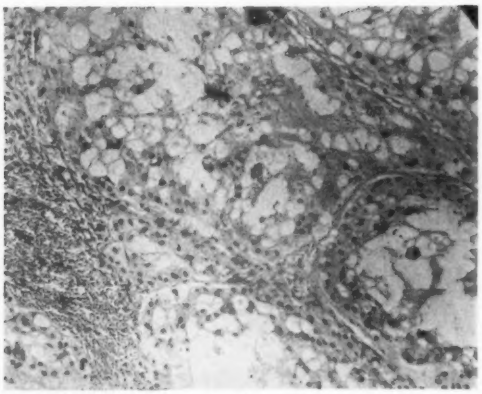
It is at present widely accepted that the best treatment of these tumors is their total resection (Mixter and Mixter, Mabrey), because as a rule they are radioresistant. The evolution of the case corroborates this point of view:

A 54 year old male suffered a direct trauma over the sacrum 2 years before admission. This was followed by persistent pain which became progressively worse until he was unable to work and sleep.

Fig. 3a.

A few months later he developed some rectal trouble and a "so called" rectal abscess was incised. The patient was relieved for 3 months, following which the sharp, stabbing pain reappeared. Two weeks before admission the patient complained of radiating pain along the outer aspect of the leg and foot, with a sensation of numbness in the outer aspect of the thigh.

Fig. a.



b

Fig. 4. a, Chordoma destroying the sacrum. b, Microscopic aspect, lower power.

The local physical examination showed marked spasm of the sacrospinalis muscle and a swollen and acutely tender area covered by edematous skin extending from the fourth lumbar vertebra down the entire left buttock. Rectal examination showed the presence of some tenderness over the sacrum and coccyx. The roentgenograms showed the distal portion of the sacrum to be markedly destroyed by an osteolytic process that involved both sacral walls (Fig. 4a).

The diagnosis of chordoma was made first by an aspiration biopsy. The surgical biopsy confirmed the diagnosis. Histological studies showed the presence of basophilic cells with large nuclei and finely vacuolated protoplasm. The borders of the cells were indefinite, and some of them appeared very distended. Many signet-ring forms were present. No mitosis was observed, but there was considerable nuclear pleomorphism.

The tumor was considered to be too widespread to be surgically removed; roentgen irradiation treatments were given. In spite of this treatment, the tumor continued to increase in size. Although the patient had temporary relief of his pain following each treatment, neurological signs of cauda equina

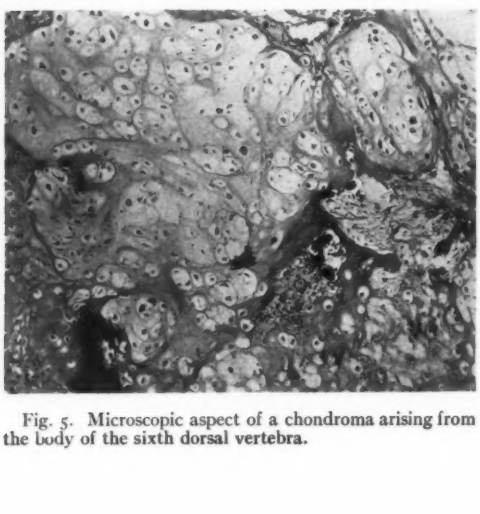


Fig. 5. Microscopic aspect of a chondroma arising from the body of the sixth dorsal vertebra.

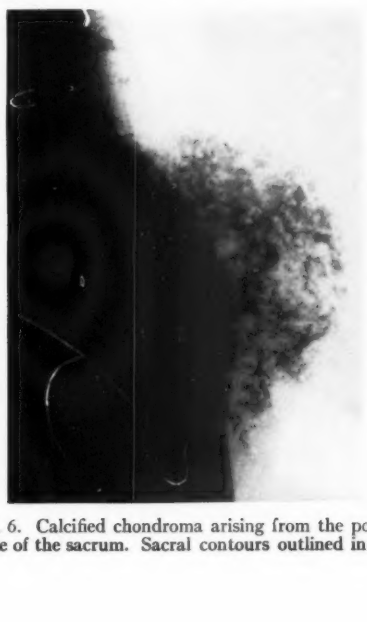


Fig. 6. Calcified chondroma arising from the posterior surface of the sacrum. Sacral contours outlined in white

a

b

Fig. 7. a and b, Fibrosarcoma involving the neural arches of several lumbar vertebrae. The upper portion of the tumor is calcified. c, Microscopic aspect of the tumor, high power.

compression and root involvement appeared. Locally, a hard mass of osseous consistency could be palpated in the buttock.

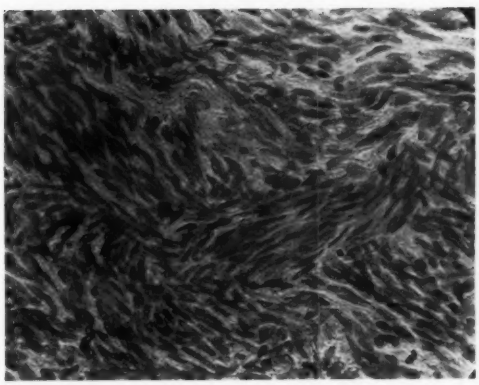
In order to relieve the pain it was necessary to perform a chordotomy. No metastasis could be observed after several roentgenographic examinations. The patient died 2 years after first admission.

CHONDROMA

Benign cartilaginous tumors arising from the neural arches have been frequently reported (Paulian and Bistriceano, Rix and Geschickter). Chondromas arising from the vertebral body itself are considered less frequent. The patient studied by us is of particular interest. The evolution of his cartilaginous tumor seemed to corroborate the statement made by Geschickter that the prognosis of chondromas is not dependent upon the histological picture but upon their localization:

A 45 year old female on admission complained of sharp pains of 9 months' duration over her right chest, associated with the respiratory movements. The intensity of the pain had been progressively increasing.

On admission, the physical examination was inconclusive. Roentgenograms of the dorsal spine, taken following induced pneumothorax, showed the presence of a mass at the lateral side of the body of the sixth dorsal vertebra. A few days later a laminectomy was performed, and a tumor the size of an egg arising from the body of the vertebra and projecting inside the pleural cavity was found. Anatomopathological studies showed the presence of a chondroma (Fig. 5).



c

Following resection, she was very well for about 1 year when the same type of symptoms, but with greater intensity, reappeared. Repeated roentgenograms showed the recurrence of the growth at the same level. At operation a mass the size of a golf ball was found in the same previous localization. A very careful complete removal of the tumor was performed and microscopical studies showed a typical chondroma without signs of malignancy. After operation, roentgen therapy was instituted.

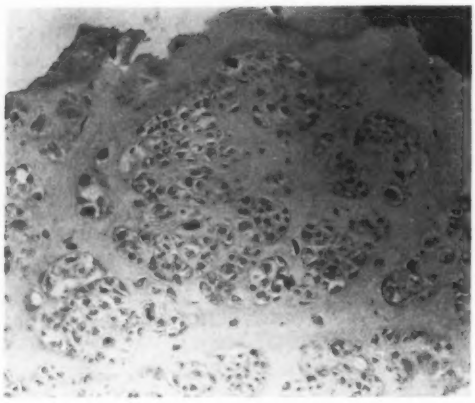


Fig. 8. Microscopic aspect of a chondrosarcoma involving the eighth dorsal vertebra.

Following the operation she was completely free from pain for only a short while. A few weeks later she started to complain of pain over the abdomen. The gall bladder and the appendix were removed without the slightest relief. A body brace was then given.

She returned after 4 years complaining of weakness and numbness of the legs, inability to walk, and numbness in the abdominal wall. Physical examination showed a paraplegia with hyperactive deep reflexes and sensory loss from the level of the fourth dorsal dermatome down to the toes. A recurrence of the tumor was detected on the roentgenograms, with destruction and mild compression of the same vertebral body. New surgical intervention was performed and a huge chondroma compressing the cord was found. The tumor completely invaded the vertebra and the ribs. Only a sufficient amount to make the spinal canal as large as normal was removed. The aspect of the tumor was unchanged on microscopical examination; no signs of malignancy could be found.

Following operation, the pain did not diminish and it was necessary, later on, to perform a chordotomy. The patient died 6½ years after first admission.

When these tumors are localized at the neural arches and grow posteriorly, they may reach enormous sizes without producing serious complications, as demonstrated by the case reported by Ljachovitzky in the cervical spine, and by one of our cases arising from the sacrum and producing an enormous growth during an interval of several years:

A 61 year old male gave a history of fall on left hip 10 years prior to admission. Six years following the fall the patient noticed a lump over the left side of the sacral region. It was never painful or tender but the patient noticed some back pain after a heavy day's work. The mass grew very slowly until 2 years before admission, at which time it began to grow more rapidly. Six months before admission there was some tenderness on palpation, the mass became swollen and began to produce a steady, aching type of pain, with short intervals of radiation down to the left leg. There was no loss of weight or appetite and the general condition of the patient remained excellent throughout.

On physical examination a hard, nodular growth measuring 15 by 10 by 7 centimeters fixed to the sacrum was found. It was slightly tender on palpation. On the roentgenograms the tumor appeared to invade the sacrum and project backward (Fig. 6).

Fig. 9. a, Multiple myeloma involving the dorsal spine.

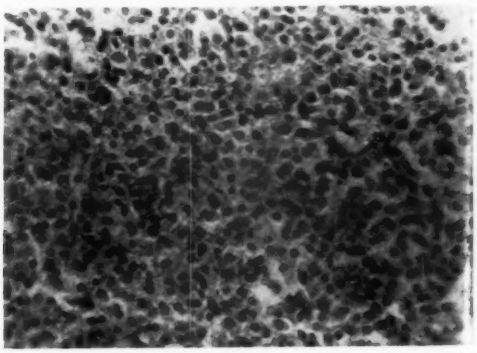


Fig. 9. b, Microscopic aspect of the tumor, high power.

Surgical removal was undertaken. During the operation it was observed that the mass was lobulated and presented areas of softening. It was chiselled away from the sacrum but a complete removal was impossible because the sacrum was deeply involved.

The histological slides showed a tumor composed mainly of cartilaginous cells. The matrix was hyaline and very abundant, much of which was calcified. In some places there was myxomatous degeneration. No evidence of malignancy was observed.

At present, 7½ years after surgical removal, the patient is in excellent general condition, works on his farm and has only occasional mild back pain.

The treatment of these tumors is total resection if possible. They usually do not respond to roentgen therapy. Good results after total removal have been reported by several authors, particularly in tumors located in the neural arches (Peycelon and Aufrere, Ljachovitzky), provided no neurological complications are present and that removal is complete.

Fig. 10. Localized destruction (arrows) of two lumbar bodies produced by metastasis from carcinoma of the breast.

FIBROSARCOMA

Seven cases of fibrosarcoma were studied. The process was localized in the lumbar spine in 3 cases; in the dorsocervical region in 1 instance. In the remaining cases the process had produced a destruction of the sacrum.

The age of the patients ranged from 3 to 73 years. Six were males. A history of definite local trauma before the onset of symptoms was found in 3 cases. The first symptom was in accordance with their localization. The

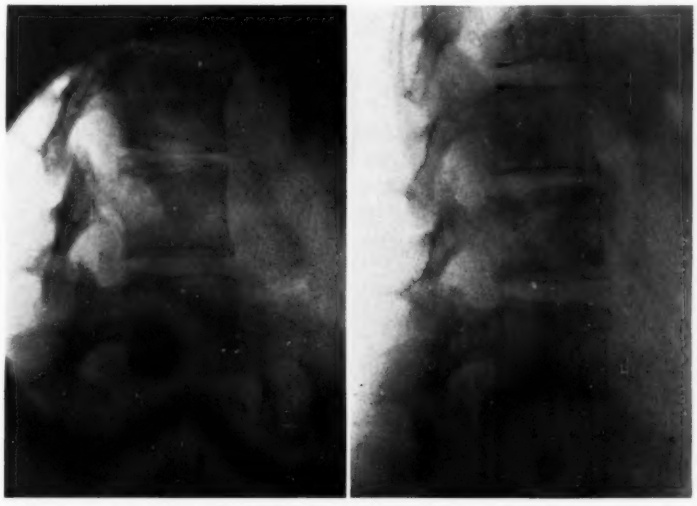


Fig. 11. a, left, Osteolytic destruction of the posterior part of the second lumbar vertebra before treatment. b, After x-ray therapy and testosterone, some recalcification can be seen. Some osteoplastic nodules can be seen in upper and anteroinferior part of the second lumbar vertebral body.

Fig. 12a.

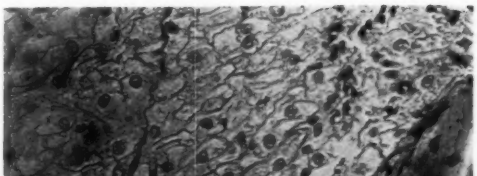


Fig. 12b.

Fig. 12. a, Collapse of a lumbar vertebral body produced by metastatic hypernephroma. b, Microscopic aspect of the tumor.

cases involving the sacrum usually presented sciatic pain; those involving the lumbar spine, usually developed low-back pain; and in the 1 case involving the cervicodorsal region, weakness of one hand was the initial symptom.

Fullness or presence of a mass in the paravertebral region or on rectal examination was present in 4 cases. Tenderness over the spine on palpation or percussion was found in 3 cases.

In the roentgenograms the lesion was seen to be purely osteolytic. It was confined to the vertebral bodies in 2 cases; to the neural arches in 1 case; to the whole vertebra in 1 case; and the sacrum and sacroiliac joint in the 3 remaining cases.

The clinical diagnosis was confirmed by aspiration biopsy in 2 cases; in the remaining ones, by surgical biopsy or at autopsy.

Fig. 13a.

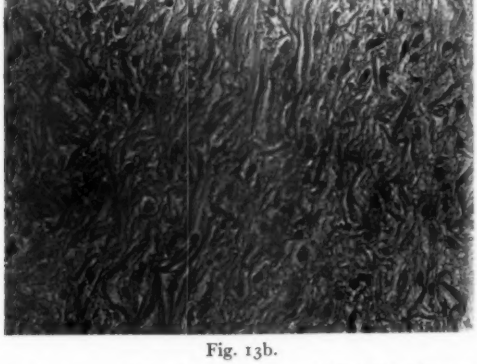


Fig. 13b.

Fig. 13. a, Perineurial fibroma involving the bodies and neural arches of the twelve dorsal and first two lumbar vertebrae. b, Microscopic aspect of the tumor. High power.

The end-result in 6 cases is known to us. Two died shortly after admission. In the third case diagnosis was incorrect and two drainage operations were performed. Later on, he was treated with x-ray radiation and died 14 months after the onset of symptoms. The fourth case was treated only by means of x-ray therapy after the clinical diagnosis had been confirmed by aspiration biopsy. The patient died 27 months after the onset of symptoms. The fifth case presented clinical signs of cord compression and it was necessary to perform a laminectomy. The patient died a few months after operation. Finally, the sixth case has been followed for over 5 years and has had no recurrences. Although some authors have reported 5 year cures in cases of fibrosarcoma involving the spine (Aviragnet and Duhem), their number is relatively small. A detailed report of our case seems justified:

This patient was a 57 year old male who 3 years prior to admission to the hospital started to have some pain localized in the middle of his back. One year later a lump the size of a silver dollar was noticed. The pain became more acute and the tumor increased in size. On admission, local physical examination showed the existence of a swelling twice the size of a fist, just lateral to the spinous processes on the right side, and extending from the tenth dorsal vertebra to the third lumbar. This mass was tender and fluctuant on palpation. Roentgenographic studies revealed the destruction of the pedicle of the first lumbar vertebra, on the right side, the presence of a soft tissue mass extending down into the lower lumbar region, and the existence of an area of calcification in the upper pole of the tumor (Fig. 7a and b).

An aspiration was performed and myxoid material obtained. Microscopic studies confirmed the diagnosis of fibrosarcoma.

A few days later surgical removal of the tumor was undertaken. The mass was moderately well encapsulated, lying in the angle formed between the spinous and the transverse processes, of the lower dorsal and upper lumbar regions. The tumor was adherent to the transverse processes of the lumbar vertebrae, making it necessary to strip the periosteum of some of them in order to remove the tumor. Before suture, 8 radium needles and 3 milligrams of radium were placed in the walls. After operation patient received x-ray therapy. At present, 7½ years after surgical removal, he is in good general condition and there has been no local recurrence.

CHONDROSARCOMA

In the case we studied, the chondrosarcoma was localized in the dorsal spine:

This 65 year old male had a history of onset of sharp pain in his right upper abdominal quadrant 7 months before admission. At first this pain appeared in attacks, occurring about once a week but progressively becoming more frequent. He lost 10 pounds. On physical examination gastrointestinal and genitourinary series were negative except for a nonfunctioning gall bladder.

One year later he started to complain of dull aches in the legs, soreness of the spine, poor bowel and bladder control, and weakness of the legs. Physical examination on readmission to the hospital showed the presence of a spinal cord compression at the level of the eighth dorsal vertebra. Roentgenographic studies demonstrated the destruction of the vertebral body of the eighth dorsal vertebra.

A laminectomy was performed and a tumor compressing the cord was found and partially removed. It had invaded the eighth rib and the right part of the vertebral body. Microscopical studies showed the presence of a chondrosarcoma (Fig. 8).

Following the laminectomy the patient received roentgen therapy with marked symptomatic relief of pain. However, he died 14 months later.

OSTEOGENIC SARCOMA

The only patient with osteogenic sarcoma of the spine seen in this hospital was a 23 year old male, admitted complaining of severe attacks of pain in the back of his neck. The pain was episodic at first, but later became constant and radiated to the right arm. Physical examination showed all the clinical signs of cord compression at the level of the sixth cervical vertebra. Roentgenographic studies were negative. Exploratory laminectomy was performed and a tumor involving the fourth, fifth, and sixth cervical vertebrae was found and only partially removed because much bleeding was encountered. The patient died shortly after the operation. At autopsy, it was observed that the tumor had completely invaded the lower cervical region.

Although microscopical slides are at present unavailable, the diagnosis of osteogenic sarcoma was definitely established at the time of the patient's death.

HODGKIN'S DISEASE

Four cases of proved Hodgkin's disease presented vertebral destruction. The process was localized either in the lower cervical or in the upper dorsal segment, with the exception of one case in which there was a generalized vertebral involvement. The clinical manifesta-

tions of these vertebral involvements were represented by radicular or local pain, or by signs of cord compression. One case developed a complete block at the level of the second lumbar vertebra, requiring a decompressive laminectomy.

The roentgenograms demonstrated that the process usually involved the vertebral bodies and the transverse processes. The lesions were always osteolytic in character. The intervertebral disc appeared thinned in one of the cases.

All our cases were treated by means of x-ray therapy. One patient had symptomatic relief for a period of 5 years. Roentgenographic follow-up during this period of time showed complete arrest of the osteolytic process.

Autopsy findings were available in 2 cases. The spongy bone of the involved vertebrae was found to be replaced by a soft tumor. This tumor was spreading over the anterior surface of the vertebrae in one case and the spinal cord in the other. In not a single instance was spinal cord compression present. At some points, several tumoral nodules localized in the posterior mediastinum appeared to be invading the vertebral bodies.

MULTIPLE MYELOMA

Ten proved cases of multiple myeloma involving the spine were studied. Autopsy findings of 7 were available.

The age of the patients at the onset of symptoms was between 40 to 78. Eight of the patients were males. While under the care of this hospital, 9 of them died. The interval between the onset of symptoms and death ranged from 4 months to 6 years. From a clinical standpoint, there seemed to be some acute forms of the process capable of producing death in a short time.

Repeated investigations for Bence Jones proteins were performed in 4 cases, and a positive finding was obtained in only 1 instance. Among the remaining cases in which these proteins were not investigated, we found that urinary albumin was present in 4 cases.

The main clinical signs were a sensation of marked fatigue and extreme lassitude that eventually confined the patient to bed. Radicular pains along the distribution of peripheral nerves and pain on pressure over ribs, pelvis, and skull were frequent manifestations. Blood studies usually showed the presence of marked anemia, sometimes accompanied by leucocytosis.

Roentgenographic findings varied from the apparition of a marked osteoporosis without definite destructive areas, to the presence of multiple and well circumscribed osteolytic lesions.

On microscopical examination it was found that the normal elements of the osseous marrow were replaced by plasma cells or by small cells with hyperchromatic nuclei and scanty pale protoplasm which resembled plasma cells.

At autopsy multiple, scattered, grayish yellow or hemorrhagic nodules were found in the spine or surrounding tissues. Tumoral tissue was present in the ribs, in the vertebral bodies or in the neural arches. In some cases the tumoral neoformation invaded the neural canal or the erector spinae masses. In 1 case the cauda equina was compressed.

SOLITARY MYELOMA

Instances of solitary myeloma producing destruction of a vertebral body have been reported by Wright, Peyton, Paul and Pohle, Pasternack and Waugh.

Among our studied 10 cases of multiple myeloma we found 2 cases in which the lesion could be considered circumscribed to the spine during the early stages of the disease. In 1 case the tumor produced compression myelitis and a laminectomy was performed (Fig 9). This patient died of secondary infection following operation and consequently we disregard the fact that the condition would have become generalized. In the second case the lesion was confined to one vertebral body during the early stages. As the patient's general condition was excellent and improved following the use of a body brace, the condition was diagnosed as Kuemmell's disease. However, roentgenograms taken a few months later, revealed the presence of a marked loss of calcium and mottling of the thoracic cage. At autopsy, two vertebrae and one rib were removed. A multiple myeloma was responsible for their destruction.

In some of the cases of vertebral solitary myeloma reported in the literature, the lesions remained confined to the spine for periods of 10 years (Cutler, Buschke and Cantril). In other instances, however, the solitary vertebral localization was a temporary feature, with multiple areas of destruction appearing several years later (Jacox and Kahn).

VERTEBRAL DESTRUCTIONS PRODUCED BY METASTASIS FROM PRIMARY TUMORS ELSEWHERE IN THE BODY

Fifty cases with vertebral metastatic lesions were found. In order of frequency they were as follows:

	Cases
Carcinoma of the breast	32
Carcinoma of the prostate	7
Hypernephroma	3
Ewing's tumor	1
Chondrosarcoma	1
Broncogenic carcinoma	1
Carcinoma of the skin	1
Carcinoma of the rectum	1
Carcinoma of the cervix	1
Fibrosarcoma of the cervix	1
Osteogenic sarcoma	1
	50

Carcinoma of the breast. The 32 studied cases included patients between 33 to 67 years of age. The majority of the lesions appeared in patients in the fourth (36.6%) and fifth decades (30%) of life.

The interval between surgical removal of the breast and the discovery of the spinal lesion varied from 4 months to 11 years.

The spinal segments involved in order of frequency were as follows: lumbar, dorsal, cervical, and sacrum.

The most frequent clinical sign was pain, either localized in the spine or radiating along the distribution of the peripheral nerve roots. Loss of weight, pathological fractures, sleep interference, etc., were frequent findings.

The roentgenograms showed purely osteolytic lesions. In one case, however, there were areas of osteolysis and areas of increased bony density (Fig. 11).

The neoplasm usually determined marked destruction of the involved vertebrae and the body collapsed in many instances. The shape of the vertebrae after their collapse varied, being wedge-shaped in the upper dorsal spine, while in the lumbar segment it was more frequent to observe accordion-like or fish-tail deformations.

In some cases the roentgenograms showed only small areas of the vertebrae destroyed by the tumor. These *localized* destructions were visible on the roentgenogram probably because of the fact that they eroded the cortical bone, whereas the vertebral body itself preserved its normal configuration (Fig 10).

In the treatment of these metastatic lesions, roentgen therapy was used for the relief of pain. Evaluation of the results could be made in 16 cases and was as follows: complete temporary relief of pain in 5 cases; partial temporary relief in 8 cases; no relief in the remaining 3 cases.

Testosterone has been used as a palliative treatment by several authors, with beneficial (Adair and Herrmann, and Fels) and harmful (Farrow and Woodard; Farrow) results. Testosterone was administered to 5 of our patients, the first trial being performed on a patient in whom roentgen therapy had failed to produce the slightest relief of her constant pain. Despite the fact that roentgenographically the lesions remained unchanged, we were able to discontinue completely the administration of morphine. This patient was under hospital observation for 1½ months and received a daily dosage of 25 milligrams of testosterone. She died 2 months after returning home.

Among the remaining 4 patients, the administration of testosterone was not beneficial in 3. In the fourth patient, testosterone produced complete relief of pain for 7 months. Later on, the pain recurred and failed to respond either to testosterone or to roentgen therapy. The roentgenograms revealed increased density of some of the previous osteolytic areas (Fig. 11, a and b). This could be interpreted as a reossification produced by the administration of testosterone. However, we should bear in mind that this patient had had previous roentgen therapy, and that reossification and sclerosis of a vertebral body following irradiation has been observed by several authors (Rix and Geschickter, Leddy, Pfahler).

Carcinoma of the prostate. Our patients with metastatic lesions from carcinoma of the prostate were between 44 and 71 years of age. The bone metastases were localized in the lumbar spine in 2 patients; in the dorsal segment in 2 patients. There was a generalized involvement of the spine and pelvis in the 3 remaining patients. The roentgenograms showed that the metastatic lesions were osteoplastic in all of them.

An evaluation of the results of roentgen therapy could be made in only 4 patients. One patient was completely relieved of pain; 2 patients had partial relief; 1 patient had no relief of pain. This last patient was later treated with stilbesterol, and 16 months after onset of this treatment, the patient feels excellent and has gained weight.

In none of our studied cases were the values of acid phosphatase (Gutman, Sproul and Gutman; Huggins and Hodges; Gutman and Gutman) recorded.

Hypernephroma. Three patients with hypernephroma developed metastasis in the spinal column. The metastatic lesions from hypernephroma were localized in the dorsal spinal segment in one case and in the lumbar spine in the 2 others. A pathological fracture was the first clinical sign in 1 patient. The patients were all over 50 years of age.

In the roentgenograms the lesions were seen to be purely osteolytic. The clinical diagnosis was confirmed at autopsy in 2 cases, and following laminectomy in the 1 remaining. In the last case, the tumor had produced a complete block at the level of the first lumbar segment and a complete destruction of the vertebral body (Fig. 12, a and b).

Ewing's tumor. A boy 16 years old with Ewing's tumor of the right femur developed generalized metastasis involving the other femur, the skull, and the sacrum. The diagnosis was confirmed by biopsy of a nodule under the scalp. The sacral lesions were purely osteolytic.

Chondrosarcoma. Our case of metastatic lesion produced by chondrosarcoma is interesting because it appeared in a patient suffering from multiple cartilaginous exostosis. It was not until the patient was 48 years old that several exostoses attached to the femur underwent malignant degeneration. The patient was treated by means of roentgen therapy for 5 years with only symptomatic relief. At the end of this period, he suddenly developed signs of cord compression and died following a laminectomy. During the operation it was observed that the cord was compressed by a mass arising from the eighth dorsal vertebra. This mass could have been a primary exostosis that had also undergone malignant degeneration, but because of the patient's clinical history it was classified as a metastatic lesion.

Broncogenic carcinoma. A case of broncogenic carcinoma was studied with a partial destruction and collapse of the body of the fourth lumbar vertebra due to a metastatic lesion. The patient was a 39 year old male with a history of low back pain for 5 months, cough and difficulty in swallowing solid food for 3 months. The roentgenograms showed, in addition to the vertebral destruction, a marked mediastinal enlargment. The patient was subjected to roentgen therapy and died 3 months afterward.

Carcinoma of the skin. Vertebral destruction secondary to carcinoma of the skin appeared in a male 62 years old who 6 years prior to admission had developed a well differentiated epidermoid carcinoma over the right temple. X-ray therapy was administered and the skin lesion healed. Four years later he noticed a small lump, 1 centimeter in diameter, in front of his right ear. Eleven months before admission, he suddenly developed pain in the upper dorsal spine. Roentgenograms taken on admission showed a compression of the sixth dorsal vertebral body. X-ray therapy was again administered without relief of pain. The patient died 1 year later.

Carcinoma and fibrosarcoma of the cervix. Both types of tumors produced osteolytic lesions in the vertebral bodies accompanied by pathological fracture, very similar to the lesions seen in cases of carcinoma of the breast metastasizing to the spine.

Osteogenic sarcoma. Sarcomatous lesions associated with elevated temperature and increased white count may sometimes be confused with inflammatory conditions. The differential diagnosis in our case was based on the clinical history:

A 34 year old male was admitted in 1936 complaining of marked pain in the right hip. The patient stated that in 1922 a lump had appeared over the second metacarpophalangeal joint of his right hand. Between 1922 and 1930 this tumor was removed 5 times because of repeated recurrences. Finally in 1930, the finger was amputated. However, there was a local recurrence of the tumor and in 1931 the right forearm was amputated 3 inches below the elbow. In 1934 the axillary glands became enlarged and were removed. Microscopical studies throughout confirmed the presence of osteogenic sarcoma.

The patient was asymptomatic until September, 1936, at which time he developed sharp pain in his right hip. The roentgenograms at this time showed marked destruction of the hip joint. A hip spica was applied to control the pain. In February, 1937, the patient developed sudden severe pain between the shoulders. A few days later there was sudden loss of bowel and bladder control, numbness from the nipple line down and severe pain on coughing and sneezing. The following day, flaccid paralysis with complete motor and sensory loss was present. Roentgenograms demonstrated a paravertebral soft tissue shadow. The patient was running a temperature of 102–103 degrees and his blood count was 68,000.

An attempt to aspirate the paravertebral mass proved unsuccessful. A laminectomy was performed and a tumor 2½ inches in diameter, moderately firm, extremely friable, fish-flesh appearance and not encapsulated was found. The vertebral bodies appeared very rough and invaded.

Following removal, roentgen therapy was instituted. The patient died 1 month after surgery.

VERTEBRAL CHANGES FROM TUMORS ARISING IN THE VERTEBRAL CANAL

Vertebral changes secondary to tumors arising in the vertebral canal have been described by several authors (Rix and Geschickter). Among our material we found 2 such cases. In 1, there was a meningioma that had produced widening of the interpedicular space of one vertebra. The other was a case of perineurial fibroma.

Perineurial fibromas have received different denominations (neurinoma, solitary neurofibroma, glioma peripherique). According to Mallory and Penfield, they arise from the connective tissue surrounding the nerve fibers, and do not contain nervous elements.

They may be intrameningeal or extrameningeal, or in some cases develop along a nerve root, thus producing the so called dumb-bell tumors. In the cervical and dorsal regions, these tumors usually produce a progressive erosion of the laminae, and give origin to great extravertebral masses. However, in the lumbar region, they frequently remain intrameningeal throughout, and produce marked erosion of the vertebral bodies and neural arches (Camp, Adson, and Shugrue) (Fig. 13).

The evolution is usually very slow, giving rise to clinical signs of progressive cord compression if they remain intrameningeal.

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CERVICOMEDIASTINAL AND MEDIASTINAL CYSTIC HYGROMAS

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CYSTIC hygroma of the neck is a well recognized entity. Gross and Goeringer, in 1939, reported a group of 27 patients, bringing the total number in the literature at that time to approximately 225 cases. Although an uncommon lesion, there are doubtless a considerable number of these cases which are not recorded in the literature; in 1946 twelve cervical hygromas were excised at The Children's Hospital. In view of the marked tendency of these cystic masses to involve adjacent structures by direct extension, one might anticipate a relatively high incidence of cervicomediastinal lesions. However, a review of the literature reveals only 19 cases of cervicomediastinal hygromas. Intrathoracic hygromas, without involvement of the neck, are even more rare. Sanes, MacManus, and Scatchard, reporting a case of cystic lymphangioma of the mediastinum in 1945, were able to find only 8 published apparently similar cases; some of these, on close inspection, were probably not true hygromas. The lack of uniformity in the treatment of cervicomediastinal and mediastinal hygromas prompts this review of the subject, with the report of 3 additional cases.

REPORT OF CASES

CASE 1. No. 293002, E. F., a 14 month old white girl, was admitted to The Children's Hospital on April 11, 1945. A mass had been present in the left side of the neck since birth, and this had increased steadily in size. Physical examination revealed a well nourished child with normal development for her age. There was a large cystic swelling on the left side of the neck (Fig. 1), in the center of which was a small, hard portion about 2 centimeters in diameter. The entire mass greatly increased in size when the child cried, and it decreased in size during inspiratory efforts. There were no abnormal physical findings related to the thorax or to the remainder of the body.

Laboratory data. The white blood count was 10,200. Urinalysis was negative. X-ray and fluoroscopic examination showed a large, round, soft tissue mass of homogenous density in the left, upper part of the chest (Fig. 2). On expiration the mass was most prominent in the neck. On inspiration the major portion of the mass could be seen in the left side of the thorax. On digital compression of the cervical mass the mass within the thorax produced a fairly marked shift of the trachea and mediastinal structures to the right. There was no definite abnormality of the lungs.

First operation. On April 13, 1945, under avertin-ether anesthesia, cervical exploration was performed. A large cystic hygroma in the left side of the neck was dissected out cleanly. It soon became apparent that the mass was a multilocular structure. There were 3 main components: one going to the base of the skull; one extending down beneath the left scapula; and a third extending into the mediastinum, probably to the level of the heart. It was impossible to remove all intrathoracic portions of the cystic hygroma through this exposure. As far as possible, the intrathoracic cysts were cut out, and the interior of some remaining ones were swabbed with tincture of iodine in the hope of producing sclerosis. A small rubber drain was inserted into the mediastinum and the cervical wound closed about the drain. Postoperatively, considerable amounts of fluid were expressed from the cervical wound daily for about a week. The child was discharged from the hospital markedly improved on the eleventh postoperative day.

Pathology report. The specimen consisted of 3 red-yellow soft pieces of tissue containing multiple clear walled cysts filled with a yellow fluid. The cysts varied in size from .1 to 1.2 centimeters in diameter. Microscopic examination revealed multiple, cystic, endothelial-lined spaces. These varied from large irregular cavities to small cysts (Fig. 3). Some contained smooth muscle in their walls; others had only connective tissue. Supportive structures contained variable amounts of fat. The findings were typical of cavernous lymphangioma (cystic hygroma).

Second admission. On August 6, 1946, 16 months after the first operation, the child was readmitted. She had made an uneventful recovery and had been relatively asymptomatic except for a poor appetite and slow weight gain until May 1946, at which time the mother noticed a swelling over the left upper chest posteriorly. The swelling appeared rapidly and was associated with some pain in the left arm. Physical examination disclosed a well healed left, transverse, cervical incision just above the clavicle. Percussion of the chest was normal except for a small area of dullness just to the left of the sternum. In the

From the Surgical and Pathological services of the Children's Hospital and the Peter Bent Brigham Hospital, and the Departments of Surgery and Pathology of the Harvard Medical School.

TABLE I.—CERVICOMEDIASTINAL HYGROMAS

Number	Author	Date	Age	Sex	Therapy	Result
1	Dowd	1913	2 yrs.	F	Resection of cervical portion and part of substernal extension. Cervical recurrence—1 mo. later—resected.	Died; postoperative hemorrhage.
2	Figi* Case 1	1929			Radium to neck lesions.	?
3	Case 2	1929				
4	Case 3	1929			No therapy to thoracic portions (?)	
5	Case 4	1929				
6	Eloesser	1931	8 yrs.	M	Resection through cervical approach	Improved
7	Martin and Lelong	1933		F	Partial resection	Improved
8	Michaelis	1934	8 mos.	M	Mediastinal portion resected.	Postoperative death
9	Singleton Case 1	1937	8 yrs.	F	Excision of cervical portion. X-rays to mediastinum	Improved. No recurrence 16 mos. later.
10	Case 2	1937	8 mos.	M	Excision of cervical portion.	Died, 10 mos. later, of infection in mediastinal part.
11	Goetsch	1938	5 yrs.	F	Excision of cervical portion. X-rays to mediastinum.	Improved. Marked reduction in size of mediastinal shadow noted 7 years later.
12	Watson and McCarthy Case 1	1940			"Operation"	Died
13	Case 2				No therapy	?
14	Arnheim Case 1	1943	17 mos.	M	Resection of cervical portion. Sclerosis of mediastinal portion.	Improved. Marked reduction of mediastinal shadow.
15	Case 2	1943	15 mos.	F	Resection of cervical portion. Sclerosis of mediastinal portion.	Cervical recurrence excised. Improved.
16	Mass. Gen. Hosp. Cabot case no. 31261	1945	13 mos.	M	Cervical part aspirated. Mediastinal part resected.	Improved. Horner's syndrome
17	Portmann Case 1	1945	10 mos.	F	Resection	Death; hemorrhage.
18	Case 2	1945	2 yrs.	M	(1) Incision and drainage of cervical part. (2) Resection of cervical portion and part of mediastinal portion. (3) Radon seeds to mediastinal remnants.	Improved.
19	Swift and Neuhof	1946	32 yrs.	M	Partially resected. Chylothorax aspirated.	Improved.
20	Gross and Hurwitt Case 1	1948	14 mos.	F	(1) Resection of cervical portion. (2) Resection of mediastinal portion. (3) Resection of subscapular portion.	Improved.
21	Case 2	1948	7 mos.	F	Resection of cervical portion. Sclerosis of mediastinal portion.	Improved.

*Two cases reported by Lemon in 1931 presumably had been included in the previous report by Figi. (Personal communication, Mayo Clinic.)

left posterior chest wall was a freely movable ovoid cystic mass measuring about 5 centimeters in its long axis (Fig. 1).

Laboratory data. The red blood count was 3,680,000 and the hemoglobin 86 per cent. Urinalysis was normal. X-ray examination of the chest showed a persistence of the shadow in the left upper portion of the chest. This extended from the superior mediastinum out into the apex of the left pleural cavity.

Second operation. On August 7, 1946, under cyclopropane anesthesia, thoracic exploration was performed. The left pleural cavity was entered through the third interspace anteriorly. In the upper part of the pleural cavity was a cystic mass somewhat larger than a golf ball; some portions of it were quite thin, whereas, others appeared to be distinctly thickened and scarred. The mass presented below the thoracic inlet and extended along the lateral aspect of the mediastinum to the root of the lung; the lung was not involved. The overlying parietal pleura was incised and the phrenic nerve dissected away from the anteromedial border of the hygroma. The vagus nerve was not adherent to the hygroma. The mass was dissected free from the aorta, the left subclavian

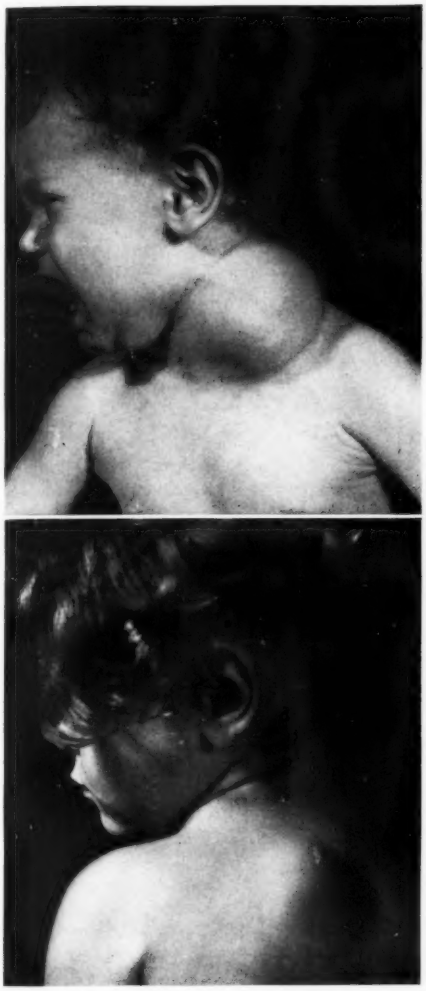

Fig. 1. Case 1. Above, Photograph of 14 months old girl with a large cervicomediastinal hygroma. The cervical swelling was prominent during crying or straining, but most of it disappeared when the child was quiet, especially during inspiratory periods. Below, Photograph 16 months after surgical removal of cervicomediastinal hygroma, now showing development of a posterior thoracic (subscapular) hygroma. (Compare with Fig. 5.)

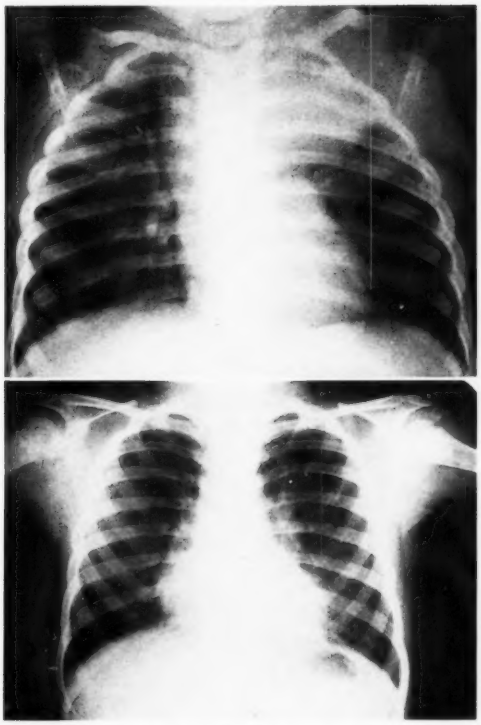

Fig. 2. Case 1. Above, Roentgenogram of the cervicomediastinal hygroma, showing the mass of uniform density in left upper part of the thorax and with a slight displacement of mediastinal structure to the patient's right. Below, Roentgenogram, following removal of thoracic hygroma.

artery, and the left innominate vein. The internal mammary artery and vein were divided and sections of them were removed with the hygromatous specimen. At the thoracic inlet some small cysts were cut across and minute bits of hygromatous tissue were left in place to avoid running the risk of injury to important anatomical structures at the base of the neck. The chest wall was closed in layers, the lung being expanded before the closure was completed. The patient stood the procedure extremely well and was returned to bed in good condition. Convalescence was uneventful. The wound healed by primary union.

Pathology report. The specimen consisted of a multicystic, reniform piece of tissue measuring 5 by 4.5 by 1.5 centimeters. Microscopic examination revealed multiple cysts, fatty and connective tissue, and numerous small blood vessels (Fig. 4). In the supporting tissues there were small nests of lymphocytes. In contrast to the cervical cysts which had been previously examined, this thoracic specimen showed a much more abundant connective tissue in the walls of the cysts.

Third operation. On August 17, the cystic mass in the left posterior chest wall was removed. This was situated deep to the levator scapulae muscle and lay on the rib cage, running out beneath the scapula. It had only a filmy attachment to the underlying

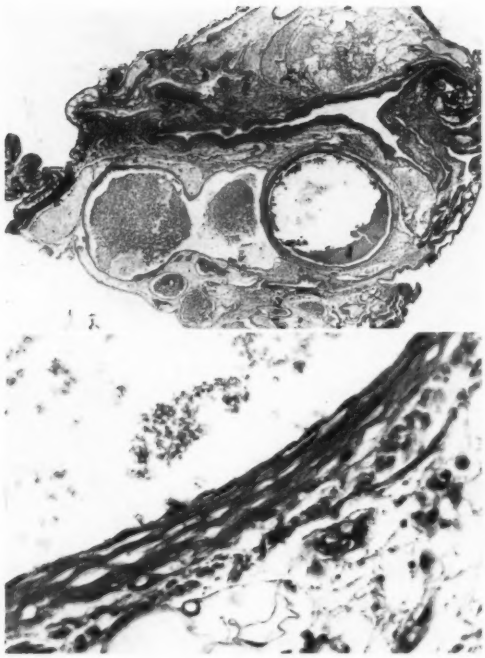

Fig. 3. Case 1. Photomicrographs of cervical component of hygroma. Above, Low power, showing the multilocular architecture. Below, Higher power, indicating the character of a cyst wall.

ribs and could be removed without difficulty. The patient tolerated this last procedure extremely well and was discharged from the hospital on the following day.

Pathology report. The specimen consisted of a cystic, irregular, egg-shaped mass measuring 4 by 2.5 by 1 centimeter (Fig. 5). The capsule consisted of dark gray, fairly tough tissue. The cyst was filled with thick, dark red-brown fluid. On microscopic examination a multicystic mass was seen, with a dense interlacing fibrous stroma. In some areas were small nodules composed of endothelial cells, with a rather high degree of cellularity (Fig. 6). There was a light infiltration of lymphocytes. Numerous large vacuolated phagocytes were present, some containing large amounts of hemosiderin, others being laden with lipoid material. The findings were those of a cavernous and capillary lymphangioma and also a more rapidly growing lymphangioendothelioma.

Follow-up note. Examination of the patient in November, 1947, showed all the wounds to be well healed and the patient to be in good condition. There was no swelling in the neck or in the left scapular region. A roentgenogram of the chest was essentially normal.

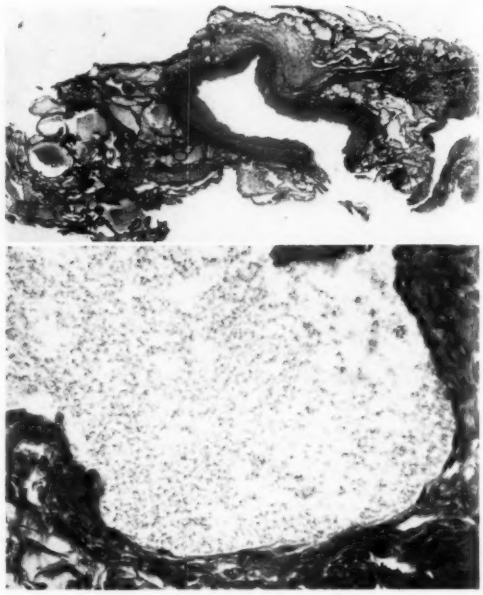

Fig. 4. Case 1. Photomicrograph of mediastinal component of the hygroma. Above, Low power, revealing the intimate relation of the cysts to large blood vessels. Below, Higher power, showing the endothelial lining of the cystic cavities.

Case 2. No. 301086, S. M., a 7 month old white female, was admitted to the Children's Hospital on January 8, 1946. The baby was born with a small nubbin of a cystic tumor on the right side of the neck, which had increased rapidly in size until now it was larger than a goose egg. The parents had noticed that the mass increased in dimensions whenever the baby cried and it would almost disappear when the baby inspired. For 2 weeks prior to admission the baby had vomited frequently and had lost 4 pounds. On physical examination a lobular, cystic mass was noted on the right side of the neck measuring about 10 centimeters in diameter (Fig. 7). This was soft and could be compressed and held down within the normal contour of the neck.

Laboratory data. Film and fluoroscopic examination showed a large, round, soft tissue mass of homogenous density in the right side of the neck. This extended through the circle of the first rib into the mediastinum and pleural cavity on the right side (Fig. 8). On deep inspiration the mass descended almost entirely into the chest, and during expiration it was very prominent in the neck. There was a moderate shift of the esophagus and trachea to the left. In a lateral view of the neck a considerable amount of the hygroma lay behind the pharynx; the trachea and larynx were markedly displaced forward (Fig. 7)

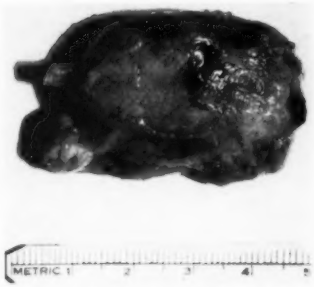

Fig. 5. Case 1. Cystic mass removed from posterior chest wall (subscapular area).

Hospital course. Because of an intercurrent respiratory infection and otitis media, operation was deferred, and chemotherapy was given.

Operation. On February 12, 1946 operation was performed under ether anesthesia. A long, transverse incision was made in a fold of the skin over the presenting mass. The platysma, sternomastoid, and ribbon muscles, as well as the omohyoid were divided. A large, irregular, smooth, multiloculated hygroma was encountered. During the operation there was a good deal of tracheal compression and intermittently there was obstruction of the airway. It seemed wisest to open the main cyst in order to collapse it. When this was done several ounces of thin, bloody fluid escaped and the respiratory difficulties completely disappeared for the remainder of the procedure. There were several large smooth walled cavities which intercommunicated, all of which collapsed when the main cyst was opened. By digital examination one could feel a finger-sized projection upward along the carotid vessels to the base of the skull. There was also a large, finger-sized projection behind the carotid sheath extending posteriorly well behind the mastoid region. Another projection went downward into the thorax and a palpating finger in the opened cyst could be passed inferiorly as far as the lung root. The mass filled about the upper third of the pleural cavity. With meticulous care all of the cyst membranes in the neck were dissected out. The removal of the membrane in the thorax seemed too hazardous, because of the danger of damaging adjacent important anatomical structures, such as the vena cava. Hence, the entire lining of this mediastinal portion of the hygroma was diffusely swabbed with tincture of iodine in the hope of destroying its lining membrane. A small rubber wick was led down into this cavity to allow for the escape of any fluid and thus permit coalescence of the cyst walls. The neck wound was closed in layers about the drain.

Postoperative course. The patient began taking fluids on the second postoperative day. She took increasing amounts of feeding without difficulty and gained 1 pound in the first 2 postoperative weeks. On 3 occasions accumulations of cystic fluid in the cervical region were aspirated, approximately 5 cubic centimeters of reddish fluid being obtained each time. The child was discharged from the hospital on the eighteenth postoperative day, afebrile and in good condition. She was last examined in November, 1947, at which time she had gained weight and looked very well (Fig. 9). The neck appeared normal. Roentgenogram of the chest showed only a slight thickening on the right side of the superior mediastinum.

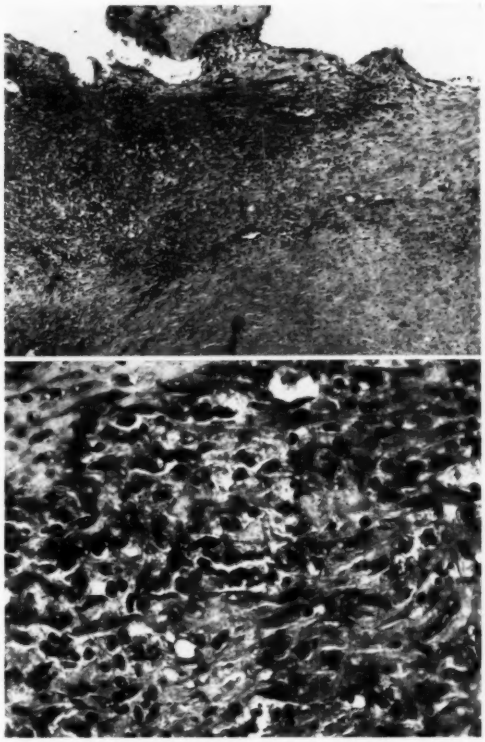

Fig. 6. Case 1. Photomicrographs from specimen shown in Figure 5. Above, The transition between simple hygroma and cellular lymphangioendothelioma is evident. Below, From endotheliomatous area, showing cellular portions differentiating into capillary spaces.

CASE 3. No. 12277, R.F., a 32 year old white, male salesman, was admitted to the Peter Bent Brigham Hospital on December 1, 1943. Seven weeks previously, attempting to enlist in the Navy, he was found to have a mediastinal shadow by routine x-ray examination. He had been completely asymptomatic. On physical examination an area of decreased breath sounds and dullness was found to the right of the sternum from the third to the fifth interspace anteriorly, extending laterally for about 5 centimeters.

Fig. 7. Case 2. Above, Photograph of 7 months old girl with a rightsided cervicomediastinal hygroma. The cervical mass varied in size during respiratory movements. Below, Lateral roentgenogram of neck, showing marked anterior displacement of trachea.

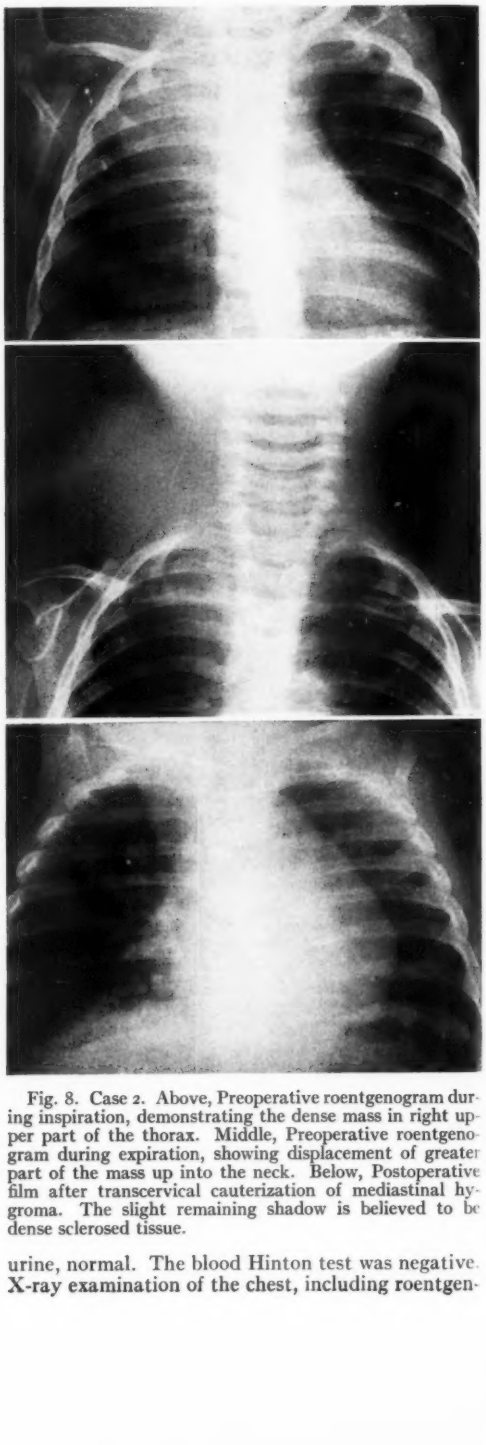

Fig. 8. Case 2. Above, Preoperative roentgenogram during inspiration, demonstrating the dense mass in right upper part of the thorax. Middle, Preoperative roentgenogram during expiration, showing displacement of greater part of the mass up into the neck. Below, Postoperative film after transcervical cauterization of mediastinal hygroma. The slight remaining shadow is believed to be dense sclerosed tissue.

No cardiac abnormalities were elicited. The blood pressure was 128/80.

Laboratory data. White blood count was 7,600; red blood count, 4,560,000: hemoglobin, 80 per cent; urine, normal. The blood Hinton test was negative. X-ray examination of the chest, including roentgen-

Fig. 9. Case 2. Photograph following surgical excision of the cervical hygroma and transcervical chemical sclerosis of mediastinal projections of the mass.

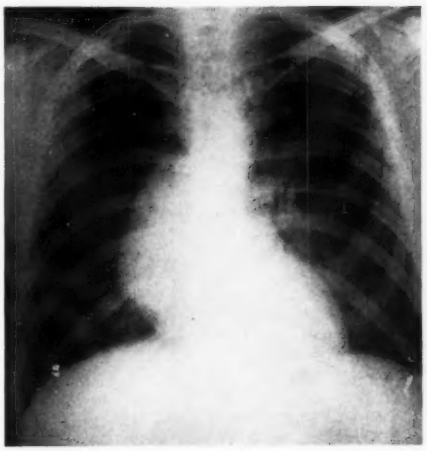

Fig. 10. Case 3. Preoperative roentgenogram of mediastinal hygroma in a 32 year old man. Right border of the mass is slightly lobulated, smoothly outlined, and obscures the right border of the heart.

okymography of the heart, showed a discrete shadow in the right anterior mediastinum suggesting a benign tumor or cyst (Fig. 10).

Operation. On the second hospital day, under positive pressure ether anesthesia, operation was carried out. The right pleural cavity was entered anterolaterally through the fourth interspace after dividing the fourth, third, and second costal cartilages. A cyst, the size of two clenched fists, bulged from the anterior mediastinum toward the right, and projected into the pleural cavity. It lay on the pericardium, to which it was lightly adherent. It reached posteriorly as far as the phrenic nerve, and extended from the diaphragm well up to the great vessels. The mediastinal pleura which covered it was divided and the cyst was freed from the mediastinal structures; there was very little bleeding during the dissection. The chest wall was repaired in layers, the right lung being completely expanded before completing the wound closure.

Pathology report. The specimen (Fig. 11) consisted of a large cystic mass measuring 13.5 by 9 by 6.5 centimeters. (Because of the escape of fluid, the original size had been larger than this.) The mass was irregularly round in shape and soft in consistency. Its external surface was pinkish-gray in color and presented a few loose fibrous, adhesive tabs. In general, the walls were thin, but in a few places they were thick and rather tough. The contained fluid was clear and amber colored. The interior of the cyst showed a multilocular structure, the various compartments of which communicated with one another. Microscopic examination showed a typical hygroma, the walls of which were formed by loose connective tissue, the spaces being lined by an endothelium.

The postoperative course was uneventful. The sutures were removed on the fifth day and the patient discharged afebrile and asymptomatic on the tenth day. X-ray examination on December 11 showed that the large mass previously noted on the right border of the heart had been completely removed.

The patient was last examined on February 21, 1944, by which time he had gained 27 pounds; he ap-

Fig. 11. Case 3. Photograph of surgically removed mediastinal hygroma.

TABLE II.—MEDIASTINAL HYGROMAS

Number	Author	Date	Age	Sex	Organs involved	Therapy	Result
1	Seidel	1904	2 yrs.		Thymus	Found at autopsy	
2	Eliaschewitsch	1929	30 yrs.	M	Pericardium	Found at autopsy	
3	Lenkeit	1929	80 yrs.	F	Epicardium	Found at autopsy	
4	Skinner and Hobbs	1936	7 yrs.	M	Inferior vena cava Diaphragm Thymus Pericardium	2 stage resection	Improved
5	Bumin	1939	25 yrs.	M	Diaphragm Pericardium	Resection	Improved
6	Sanes *et al.*	1945	59 yrs.	M	Between trachea and esophagus	Resection	Improved 1 vocal cord paralyzed
7	Watson (30, 31) and Diamond	1947	24 yrs.	M	Trachea Superior vena cava	Resection	Improved
8	Gross and Hurwitt	1948	32 yrs.	M	Pericardium	Resection	Improved

peared to be in excellent health. Three years later, upon application for life insurance, the patient had no complaints and there were no abnormal physical findings.

ETIOLOGY

These cystic hygromas may properly be classified among the congenital malformations. The lymphatic system is derived by a growth and coalescence of the lymphatic sacs or buds and their extensions. These buds develop either as outpocketings of the venous system (Sabin), or they are formed from mesenchymal deposits (Huntington). An arrest or pinching off of any part of these processes may predispose to the formation of cystic structures with the capacity for continued independent growth. The most common primary sites of hygromas, namely the cervical, axillary, and, much less frequently, the inguinal regions, coincide with the areas in which the lymphatic buds are known to be normally present in embryos.

The mechanism whereby hygromas may be found in the mediastinum, either with or without a cervical component, has not been completely explained. Eigler and Michaelis have suggested that intrathoracic lymphangiomatous cysts or cystic hygromas have grown downward from the neck. In those cases with frank involvement of both the neck and the mediastinum, such an extension would seem obvious. There are, however mediastinal hygromas with no demonstrable cervical connections. In these cases, while it is conceivable that a cervical component might have been present originally, the possibility of an independent origin within the mediastinum must also be admitted.

PATHOLOGY

Hygromas are characteristically thin-walled cystic structures lined by endothelium. Although occasionally unilocular, for the most part they are multilocular, the subsidiary cysts having a variety of sizes and shapes. Many of the cysts may intercommunicate, whereas, in other areas septation may be complete. The multilobulated appearance of the cysts in the gross is caused by these septa. Puncture of one portion of the mass with release of fluid may or may not result in collapse of the entire structure, depending on the degree of completeness of compartmentation. The fluid is usually thin and colorless; when there has been superimposed hemorrhage, the fluid may be xanthochromic or frankly bloody.

A variety of structures may be incorporated in different portions of the cyst walls, ranging from connective tissue and strands of smooth muscle to fat, blood vessels, and nerves. The most plausible explanation for the presence of foreign elements such as nerves is that suggested by Goetsch. The cysts enlarge by a process of endothelial sprouting. These buds extend along tissue planes, insinuating themselves between and around any structure in their path, and the buds subsequently enlarge to sizable cysts. In this way a vessel or nerve, actually surrounded by cystic prolongations, may appear to be traversing the cystic mass.

It is this intimate involvement of regional tissues that may cause almost insurmountable technical difficulties in surgical dissection.

A distinction between cystic hygromas and cavernous lymphangiomas has been postulated on the basis of the widespread occurrence of the latter in various regions of the body, without the development of features which have been described as characteristic of hygromas. While such a distinction may be valid in the case of lymphatic malformations in superficial areas of the body, it can hardly apply to the mediastinum. It is our belief that the terms "cavernous lymphangioma" and "cystic hygroma" describe the same pathologic process or malformation, but that the latter merely indicates a much greater tendency to development of compartments of large size.

In 1940 Lambert, during a discussion of the etiology of thin-walled thoracic cysts, pointed out the necessity of distinguishing between the multiloculated hygromas and other varieties of mediastinal cysts. He described the hygroma as being composed of a conglomerate mass of individual cysts, of differing sizes, intimately associated with various structures in the vicinity, and presenting no sharp line of cleavage from regional organs. These were contrasted with the simple monolocular mediastinal cysts, situated in relation to the pericardium, which shell out readily. Lambert considered the latter so-called endothelial or celomic cysts to come from embryologic derivations in the formation of the pericardium, and concluded that some of the cases previously regarded as mediastinal cysts of lymphatic origin probably belonged to this category. The reports of Dufours and Mourrut, Pickhardt, and of Eigler are examples in point.

CLINICAL FEATURES AND DIAGNOSIS

Hygroma of the neck usually is noted at birth, although a later onset is sometimes seen. The soft, poorly defined swelling is most commonly present in the posterior cervical triangle, although the mass may appear anywhere from just above the clavicle to beneath the mastoid process. Extension from the neck to the axilla or into the floor of the mouth has been noted, as has an engirdling prolongation beneath the mandible from one side of the neck to the other. Aside from the unsightly appearance of such a mass, associated symptoms are usually few, unless there should be sufficient displacement of the trachea or esophagus to cause interference with breathing or swallowing. When a cervical hygroma is small, it must be differentiated from other causes of cervical swelling, such as a branchial or thyroglossal cyst, lipoma, deeply situated hemangioma, lymphadenopathy, or herniation of the lung. When a cervical hygroma is large there is little difficulty in recognizing it because of its great size, its thin walls, its translucent character, and its soft, flaccid consistency.

Recognition of a cervicomediastinal hygroma is made by physical examination of the cervical swelling, supplemented by roentgenographic examination of the chest. A soft tissue shadow in the neck connecting with a mass in the mediastinum or upper pleural cavity should suggest strongly a common etiologic background. Periodic fluctuation in size has frequently been observed in cervical hygromas. This is even more characteristic of the combined cervicomediastinal lesions, in which the cervical component may be seen to increase in size during acts of crying, grunting, or expiratory efforts, and conversely to decrease in size during inspiratory movements. X-ray film and fluoroscopic examination may show descent of the mass into the mediastinum on inspiration, whereas, there is a prominence in the neck during expiration (Fig. 8). Lateral and anteroposterior films of the cervical region will reveal the direction and extent of displacement of the regional structures. Although the thoracic prolongation may extend only into the superior mediastinum, descent to a level as low as the eighth thoracic vertebra has been recorded by Arnheim. There has been no consistent correlation between dyspnea or dysphagia and the presence of a mediastinal component, these symptoms being an indication of the degree of mechanical compression which is present in a given case.

The finding of chylothorax by Swift and Neuhof associated with a cervical hygroma, and suggesting lymphangiomatous involvement of the thoracic duct, is unique. These authors again point out the relationship between an upper respiratory infection and the

onset of acute symptoms in a case of hygroma. In a young subject a hygroma may become the focal point for the development of either a severe regional infection or a widespread sepsis, and constitutes a strong reason for instituting therapy before such complications can occur.

Cystic hygromas which have been confined to the mediastinum have usually been discovered either at autopsy, or as unanticipated findings during x-ray examinations. This lack of symptomatology is probably related to the soft and yielding nature of the cysts which can obtain considerable size without giving sufficient pressure on regional organs to produce symptoms. An exception to this generality is provided by the report of Skinner and Hobbs, who described a boy with dyspnea, orthopnea, nonproductive cough, and "tightness" in the chest.

While the roentgen film may demonstrate a slightly lobulated, smoothly outlined mass, it is usually not possible by this means to distinguish hygromas from other benign tumors or cysts of the mediastinum, such as duplications of the esophagus, bronchial cysts, dermoids and teratomas, pericardial celomic cysts, or tumors of the thymus gland (Laipply).

As the result of the roentgen survey of millions of young men and women during the war years, one might have expected the detection of an appreciable number of mediastinal hygromas. In this light it is surprising to note that Blades, in his report of 109 patients with mediastinal tumors collected from various Army chest centers, found no hygromas; it is possible that some of the pericardial cysts included in his series might have been hygromas. The publication by Watson and Diamond (31) on surgical thoracic tumors in Navy personnel lists only one cystic hygroma. (The fact that a mediastinal shadow constituted a lesion which disqualified a subject from military duty may have been an explanation for the rare appearance of thoracic hygromas in the previously mentioned series which were gleaned from military personnel.)

TREATMENT

The presence of an unsightly mass in the neck of a child provides an obvious source for parental anxiety, and it is for cosmetic reasons that a surgical consultation is most frequently requested. In more rare cases, the presence of acute symptoms, resulting from compression of mediastinal structures or of the cervical part of the trachea, demand immediate surgical intervention. Arnheim reported a case in which relief from asphyxia was so imperative that operation was performed by Neuhof immediately after admission to the hospital, with the child in a sitting position, and without the use of inhalation anesthesia.

In addition to the cosmetic considerations and to the occasional relief of respiratory embarrassment, it is important to remove hygromas to prevent complications which are so apt to occur in the untreated lesions. Hygromas frequently become infected in the course of respiratory infections. While such infections may subside under chemotherapy, or after incision and drainage, the risk of an overwhelming local or blood stream infection is great. One of Singleton's patients (Case 28) died of infection in the mediastinal portion, 10 months after the cervical component had been resected. While it is true that infection is sometimes followed by local fibrosis and disappearance of the mass, such a favorable outcome is seldom encountered and it does not justify an attitude of "expectant" treatment. Spontaneous or posttraumatic hemorrhage into a cyst may result in marked distention of the same, give sudden appearance of tracheal compression, and lead to a surgical emergency. While the occurrence of malignant change in a hygroma has not been reported, this theoretical possibility adds another indication for prophylactic therapy.

There has been little difference of opinion concerning the proper approach to the lesions which are confined to the mediastinum. Exploratory thoracotomy offers the surest means for making a differential diagnosis, and certainly gives the best opportunity for definitive treatment. Fortunately, mediastinal hygromas can usually be excised with little difficulty because well developed tissue planes around the cysts facilitate their enucleation. Certainly, when a hygroma bulges well out into either pleural cavity, its surgical removal is not apt to be difficult. However, when a cysti

mass insinuates itself between mediastinal structures, the dissection might be hazardous —a fact commented upon by Sanes and his associates when dealing with a hygroma lying between the trachea and esophagus. In treating hygromas, one must be always mindful of the excellent studies of Goetsch who pointed out the tendency of a hygroma to enlarge and to envelop structures (particularly nerves and blood vessels) which lie in its path. Thus, nerves, such as the vagus and phrenic, may become completely surrounded by hygromatous tissue. To maintain the integrity of such nerves, it is frequently necessary to leave minute bits of hygromatous tissue along their surfaces, but this does not necessarily militate against a successful outcome, since an extensive experience with surgical treatment in cervical hygromas has convinced us that small remaining islands of lymphangiomatous tissue will probably become sclerosed and will not give rise to subsequent troubles.

Cervicomediastinal hygromas are apt to be much more difficult to treat than are those cysts which are situated completely within the thorax. Provided there are no complicating factors which require immediate attack on the intrathoracic portion, the combined lesions are best handled by first directing attention to the cervical part, which should be treated by meticulous dissection and removal of the cyst or cysts, having due regard for preservation of important anatomical structures. This choice of action provides the advantage of being able to continue the dissection down through the thoracic inlet to remove all or part of the hygroma which resides in the chest. The feasibility of this technique was commented upon by Eloesser, Martin and Lelong, and Swift and Neuhof; it is further indicated by the favorable use in our first and second cases. If the hygroma has previously made a large opening through the thoracic inlet, this provides an avenue of considerable width for carrying the surgical dissection downward to remove the intrathoracic projections, provided the latter are not too large and are not attached to mediastinal viscera. Under favorable circumstances, it might be possible to remove all of the intrathoracic part of the hygroma. More frequently it will be found that considerable remnants remain within the chest and can be treated by (1) leaving them for a more adequate and a wider exposure through a subsequent thoracotomy (our case 1), or (2) continuing the initial operation by introduction of sclerosing agents down through the cervical wound (our Case 2). By this latter technique remaining cysts in the thorax can be broken into (via the cervical wound) and can be swabbed out with some irritating substance (such as tincture of iodine) to destroy the lining membranes. If such cauterizing substances have been used, a soft rubber drain should be led down into the depths of the wound and left in place as long as there is any drainage in the postoperative period. (Failure to insert a drain will almost certainly be followed by postoperative reaccumulation of fluid within the cystic spaces and a reappearance of a smooth lining in many of them. In contrast, the institution of external drainage will allow the inflamed walls of the cavities to coalesce and the spaces will thereby be obliterated.)

While we recommend treatment of cervicomediastinal hygromas by (1) separate operations in the neck and thorax and (2) by excision of the cervical portion and simultaneous sclerosis of the intrathoracic part—and have been completely satisfied with the result in either instance—it is well to call attention to the favorable results reported by Singleton and Goetsch wherein excision of the cervical portion was followed by x-ray therapy to the mediastinum and also the procedure described by Portmann wherein radon seeds were applied to the mediastinal remnants.

SUMMARY AND CONCLUSIONS

The clinical and laboratory findings of cervicomediastinal and mediastinal hygromas have been reviewed. The successful management of 2 additional cases of cervicomediastinal lesions and 1 mediastinal cyst is reported.

The cervical portions of hygromas are best treated by a meticulous dissection and removal of the cystic structures. Whenever possible, treatment of the thoracic lesions is preferably done by complete extirpation of the presenting mass. Under some circumstances, a cervicothoracic hygroma can be treated by

surgical excision of the cervical portion and transcervical approach to the intrathoracic portion, the latter being treated by intense chemical sclerosis followed by external drainage. If such therapy is followed by persistence or recurrence of the intrathoracic component, thoracotomy for excision of the remaining hygroma is indicated.

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URETHRAL CARUNCLE

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URETHRAL caruncle was first described by Sharp in 1750. Since his first description of this condition there has been much controversy concerning its etiology, pathology, classification, and treatment. This diversity of opinion concerning a clinical entity which is so common stimulated our interest to investigate this subject. Accordingly, we have made a clinical and pathologic study of 120 cases of urethral caruncle. The results of this study, together with a review of the literature on this subject, form the basis of this paper. Inasmuch as a complete review of the literature on this subject has not been made for a number of years, our review has been made comprehensive.

REVIEW OF THE LITERATURE

Embryology and anatomy. According to Arey the caudal segment of the cloaca that separates from the rectum becomes the primitive urogenital sinus. In the female the originally short neck between the bladder and the urogenital sinus elongates into the permanent urethra.

The gross anatomy of the female urethra is well described by Williamson and Atlee.

The female urethra is a narrow membranous canal, about 4 centimeters long, extending from the internal to the external urethral orifice. Its diameter when undilated is about 6 millimeters. However, the caliber is not uniform, the urethra being somewhat fusiform in shape. It is capable of great dilatation. The female urethra is located behind the symphysis pubis, imbedded in the anterior wall of the vagina, and its direction is obliquely downward and forward; it is slightly curved with the concavity directed forward.

The external urethral orifice is usually shaped like an inverted V and is situated directly in front of the vaginal opening and about 2.5 centimeters behind the glans clitoridis on the summit of a small eminence. Around the meatus are seen a number of small apertures which are the openings of the periurethral glands. Skene's glands usually open on the floor of the urethra some little distance from the meatus. Each aperture is surmounted by a small hoodlike fold of mucous membrane, so arranged that the orifices are valvular in nature.

When the urethra is opened longitudinally it can be studied thoroughly. The lining membrane is found to be thrown into longitudinal folds which are close together at the meatus but radiate outward from one another as the urethra widens. The number of folds seen is variable but is usually five. In the region of the meatus these folds are united by a number of transverse ridges, thereby forming numerous crypts or depressions into which open the large urethral glands.

The peculiarly rich vascular supply which the urethra possesses is contributed to by the internal pudendal, the inferior vesical, and the vaginal arteries. The plexus of Santorini above, and the plexus of veins surrounding the base of the clitoris below lie in close relationship with the urethra. Together with their communications they constitute an investment of venous spaces throughout the greater part of the length of the canal. The lymphatics drain into the inguinal and pelvic nodes.

The nerves are derived from the hypogastric plexus of the sympathetic and from the sacropudendal plexus.

Histology. The histologic characteristics of the female urethra are well described by Maximow and Bloom, by Smith and by Gray.

The urethra consists of three coats: (1) mucous, (2) submucous, and (3) muscular.

1. The mucous coat is pale; it is continuous externally with that of the vulva and internally with that of the bladder and, as mentioned previously, is thrown into folds. The epithe-

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lium varies considerably in different individuals; near the bladder it is usually transitional and the remainder of the urethra is lined mainly by stratified squamous epithelium, with areas of stratified columnar or pseudostratified epithelium.

2. The submucous coat is very vascular, capillaries and large blood spaces abounding. Some of these are located close to the epithelium and in some cases encroach on the basement membrane. Microscopically, the submucous coat is found to be composed of a loose connective tissue with an abundant elastic network which is provided with a highly developed system of venous plexuses and has, therefore, a cavernous character like the corpus spongiosum. In this coat the urethral glands are found. Each one has a number of branches which communicate with the surface by a common duct. The glands usually have a distinct lumen but occasionally they appear in section as solid masses or columns of cells. They are found throughout the circumference of the urethra and are not limited to the posterior wall as some authors have stated.

3. The muscular coat, part of which is continuous with that of the middle circular layer of the bladder wall, extends the whole length of the tube and consists of a nonstriated internal longitudinal layer and a nonstriated outer circular layer. The involuntary sphincter of the urethra or bladder is formed by additional muscle fibers which partly surround the posterior portion of the urethra at the internal orifice. Between the layers of the triangular ligament, or urogenital diaphragm, the canal is surrounded by a layer of superficial, striated, voluntary muscle fibers, the compressor urethrae or sphincter urogenitalis.

Etiology. Since Sharp's original article in 1750 in which urethral caruncle was mentioned, many hypotheses have been offered to explain the causation of this condition. No one hypothesis or group of hypotheses has offered a satisfactory explanation; therefore, most of them will be mentioned in this paper.

Gregoire gave the following explanation based on the embryologic development of the urethra. The meatus and urethra are formed from different anlagen, as are the anus and rectum, and the hymen and vagina. The corpora spongiosa form a ring around the orifice of the urethra as well as the vagina. In the process of embryologic development this ring becomes fibrous in the greater percentage but persists in others (Pozzi).

Répiton-Préneuf theorized that the various causes of congestion in the female genital apparatus are contributing factors to caruncle formation. Simpson stated that "caruncles resemble internal hemorrhoids." Richet and Hutchinson agreed with this and felt that their origin is similar. Goodell thought very much along the same line. He stated that congestion of the urethral plexus of veins, as from overdistension of the bladder, pressure of the gravid or displaced uterus or like causes, is largely responsible, the condition resembling hemorrhoids in its origin. In Rose's opinion caruncles are associated with urethroceles which have a direct bearing on their etiology.

Ferrier based the causation of urethral caruncle on ruptured cysts of Skene's ducts. He brought out the point that caruncles practically always occur on the lower margin of the urethral meatus, just where Skene's ducts open. Carter stated that rupture of retention cysts of Skene's ducts is a causative factor. Olcott also expressed the belief that Skene's glands play a major part in the formation of urethral caruncles.

Gutierrez discussed infection and chronic inflammation—in the form of leucorrhea, pads used during menstruation, erosions, traumatism incidental to coitus and childbirth, and lack of proper local hygiene—as the chief causes of urethral caruncle. According to Gregoire the retention of droplets of urine in the urethral canal as well as of normal or abnormal secretions is a probable source of chronic urethral irritation. Olcott emphasized childbirth as a cause on the basis of its relationship to infection. Crenshaw stated that from his study only one definite conclusion as to causation could be drawn. This is that urethral caruncles seem to be secondary to a chronic irritation or ulceration of the urethral mucosa. Much emphasis was placed by early writers on gonorrhea as the causative factor.

McKim, Smith, and Rush stated that the cause of urethral caruncle has never been def-

initely proved. They attempted to correlate the pathologic with the clinical findings without much success. They drew the following conclusions from their 202 case studies:

1. Vaginal discharge, specific or otherwise, and sanitation can be eliminated as having little or no bearing on the direct causation of caruncles.

2. Some caruncles were found to be the direct result of trauma.

3. Intraurethral caruncles frequently were found behind tight urethral meatuses.

Novak (31) offered the following explanation:

1. The caruncle develops from an ectropion of the posturethral wall and is caused by postmenopausal shrinkage of the vaginal tissue.

2. All the further changes of the everted mucosa are secondary and are caused by the altered environmental conditions.

3. There is no relationship to former inflammation of the urethra or the bladder.

Symptomatology. There are few lesions of the entire body which have had so many terms used to describe them. This is based on the symptoms, which are out of all proportion to the size of the lesion.

One of the most common symptoms is severe pain, which has been described as "scalding," "stabbing," "shooting," "cutting," and "burning." It has been variously described as being referred to genital organs, hypogastrium, perineum, kidneys, rectum, bladder, lumbosacroiliac region and soles and heels of feet. The pain is said to be produced by micturition, sitting, walking, coitus, touch, menstruation, and friction from clothing, napkins, and so forth. Levant and Gutierrez stated that the pain is occasionally so great that the patient puts micturition off until the urge becomes unbearable, leading to dribbling, and incontinence. Occasionally the discomfort is so great that it leads to neurasthenia, loss of weight, insomnia, despondency, melancholia, and other mental disturbances. On the other hand some caruncles are painless.

Another prominent symptom of the urethral caruncle is bleeding. The blood is usually seen at the beginning or end of urination, following coitus, friction from clothes or pads, following trauma, and on toilet tissue. It is usually spotty —that is, there are only a few drops at a time— but occasionally it may be so profuse that the patient thinks she is menstruating irregularly. The first noticeable finding may be a small tumor mass and this may be the only symptom which brings the patient to the physician. Other symptoms are division of the urinary stream, urinary frequency, nocturia, and pruritus. Any one or all of the foregoing symptoms may be present. The duration of these symptoms is very variable; for example, in Walther's series they varied anywhere from 48 hours to 20 years.

Clinical picture and classification. This lesion occurs only in the female urethra. It is found almost exclusively between the ages of 20 and 60 years, although rarely it has been reported in children. Gutierrez reported that 33 per cent of his series of 27 patients were multiparas between 50 and 60 years of age. Walther reported 65 cases in which the patients were between the ages of 23 and 84 years and only 1 patient was unmarried.

The gross appearance of urethral caruncle has been described as vividly as the symptoms. Herman, in an excellent clinical lecture in 1892 on urethral caruncle, described it as a bright red growth like a miniature "cock's comb" or like a very small raspberry springing from the lower margin of the meatus urinarius. It has since been variously described as "a small pink or red growth with an irregular surface and vascular consistency" by Walther, "a small benign polypoid growth" by McKim, Smith, and Rush, "a small, red, pedunculated or sessile, vascular tumor" by Stevens and others.

The size may vary from that of a pinhead to that of a walnut but the caruncle is usually the size of a pea. It is usually single but may be multiple.

Urethral caruncles may be classified according to location, gross appearance, and microscopic appearance. Gutierrez divided them into three topographic types: (1) those external to the meatus, (2) those internal to the meatus, and (3) mixed, those partly within and partly outside of the meatus. Stevens classified them as sessile or pedunculated in appearance. Novak (30) stated that there are three chief types based on the histologic struc-

ture: the granulomatous variety made up of granulation tissue; the papillomatous variety which has the general structure of other papillomas, with a lobulated, treelike pattern; and the angiomatous or telangiectatic variety, which differs from the second type only in the richness of the stromal blood vessels.

Differential diagnosis. The term "urethral caruncle" has become a clinical wastebasket into which most lesions of the urethra are placed. There are almost as many terms for describing urethral caruncles as there are articles on the subject. There has been a tendency for physicians to remove urethral growths as an office procedure and simply call them "caruncles" and forego any pathologic study. This has led in many cases to what is called a "caruncle becoming malignant," because at a later date a biopsy revealed "carcinomatous changes." To be certain of the diagnosis, microscopic examination of the tissue is imperative.

There are certain lesions of the urethra from which caruncles must be differentiated:

1. Urethral polyp is usually multiple and lies well up in the urethra. It is cystic, being filled with watery fluid.

2. Urethral papilloma is a definitely benign pluriglandular growth which may arise from any portion of the urethra.

3. Urethral prolapse—that is, prolapse of the urethral mucous membrane—is a relatively common condition and is often termed "urethral caruncle." (This condition is included to make the differential diagnosis complete as presented by some authors, even though, as will be shown, our conclusions are not in agreement.) Urethral prolapse as a rule involves the entire circumference of the external urethral orifice. The tissue is pink to red, usually smooth and pouts from the urethra. It may be sensitive but not as much so as the majority of urethral caruncles and bleeding is not a common complaint. According to Ferrier, actual shortening of the urethra may be apparent on endoscopy. This condition has been treated on innumerable occasions for urethral caruncle and when greater prolapse occurred after operation, it was attributed to recurrence of "urethral caruncle."

4. Urethral varicosities are supposedly bluish, of elastic consistency, and readily reduced under compression.

5. Periurethral abscess as well as abscess of Skene's glands may strongly suggest a caruncle. The location in some cases may be almost identical and a tumor mass may be demonstrable with the symptom of marked tenderness. This lesion is definitely of an inflammatory character, presenting a purulent discharge, increased heat, swelling, and tenderness. It does not present the raspberry appearance so characteristic of the urethral caruncle.

6. Urethral carcinoma may be indistinguishable grossly from urethral caruncle in the early stages; that is, definite diagnosis will depend on microscopic examination. Statistically one is safer to call a lesion of the urethra caruncle because primary carcinoma is infrequent, whereas caruncle is relatively common.

Walther emphasized the fact that primary carcinoma of the urethra is not as rare as most of us think. The age incidence of carcinoma of the urethra is the same as that of urethral caruncle. We must remember that these lesions can and do coexist and that urethral caruncles are not necessarily precancerous lesions. All of the symptoms which characterize the urethral caruncle may be present in a malignant lesion of the urethra. From this it is evident that the final differential diagnosis is left with the pathologist.

7. Urethral condyloma has to be included because it is seen and occasionally is confused with urethral caruncle. It has a warty and fungous appearance with a smooth skinlike surface. These lesions are usually multiple and are painless. The history may be of definite help in the diagnosis.

8. Urethral diverticula and urethroceles can be definitely identified and differentiated by urethroscopy.

Histopathology. Urethral caruncle is a clinical rather than a pathologic term. However, the condition is by no means rare and therefore constitutes a rather common diagnosis for the pathologist. The histologic structure is not constant, a fact which explains the diversity of pathologic terms used to designate urethral caruncles as papillary angioma, vascular polyp, capillary angioma, urethral hemor-

rhoids, adenoma, granuloma, and others. The marked vascularity and inflammatory reaction are most commonly noted and mentioned. The controversy as to whether the urethral caruncle is always benign or potentially malignant still exists.

According to Bell, the urethral caruncle is a vascular growth of the meatus and may be either pedunculated or on a broad sessile base. It is a chronic inflammatory lesion composed chiefly of dilated vessels and plasma cells. The surface is covered by stratified epithelium and glands are present in the growth. It *may be* mistaken for carcinoma. Caruncle is a fairly common lesion but carcinoma in this situation is very rare.

Boyd agreed essentially with the foregoing, as did Karsner.

Foot described the caruncle as taking one of two forms: it may be granulomatous and belong to the category of chronic inflammations, or it may be adenomatous and constitute a small adenoma, in which case it is a neoplasm. The granulomatous type is a loosely knit mass of almost telangiectatic granulation tissue containing many leucocytes of the type that usually responds to chronic inflammation. The epithelial type may be adenomatous or it may take a papillomatous form and resemble an exaggerated leucoplakia or verruca.

Olcott stated that in 5 of his 23 reported cases, epithelial "infolding" was found to a notable degree. This aroused suspicion that the growth was not entirely benign. The absence of definite invasion of subjacent structures, uniformity as regards size and appearance of epithelial cells and the fact that mostly they were properly oriented were all features which should dispose of the suspicions.

Ferrier, Levant, Gutierrez, Carter, and Meaker agreed with what has been quoted here. Quigley reported that of his 25 cases only 2 presented evidence of malignancy. McKim, Smith, and Rush reported 202 cases without evidence of malignancy. Walther emphasized how imperative histologic study of urethral caruncles is in order to exclude urethral carcinoma, which he insisted is by no means rare.

Auer identified the urethral caruncle as the predisposing factor in some of his cases of urethral carcinoma. Menville and Counseller reported a case in which a urethral malignant lesion was preceded 14 years earlier by a peculiar type of urethral caruncle.

Everett agreed with Bell that urethral caruncle may suggest carcinoma but explained that on more careful examination the uniformity of cell structure and lack of nuclear activity leave little doubt as to its benign nature.

Friedman and Ash also agreed as to the benign nature of the caruncle.

Treatment. It is important to realize that some caruncles respond to any treatment regardless of whether it is conservative or radical. Therefore, for a true evaluation of treatment numerous patients should be treated and followed up. The method of treatment has varied little since 1857, as revealed by the following quotation from Scudder's *Diseases of Women:*

> No means that may be made use of will have the least effect, until the tumor is removed; this may be done by ligature, caustic, the knife or scissors. . . . Whatever means is adopted for removal of the tumor, without the base of it is destroyed by caustic, it will rapidly reappear; as soon, then, as the tumor is removed, whether by the ligature or scissors, its base should be destroyed, either by the application of nitric acid or a solution of the chloride of zinc carefully shielding the adjacent parts from injury. This should be repeated, at intervals, until the disposition to reproduction has entirely ceased.

The methods of treatment presented in the literature will be summarized in this paper:

I. Conservative treatment
  a. Topical application of caustics, such as silver nitrate or phenol, or soothing salves
  b. Radium and roentgen therapy
II. Radical treatment
  a. Simple fulguration
  b. Simple excision
  c. Removal with an electrosurgical knife or electric cutting loop *or* destruction with an electric needle
  d. Urethroplasty
III. Combination of conservative and radical methods
  a. Simple excision and cautery
  b. Excision and radium or roentgen therapy

Conservative treatment. a. Topical application of caustics has been used for a long time, as evidenced by the foregoing quotation. Such medications as silver nitrate, phenol, or acid nitrate of mercury (liquor hydrargyri nitratis

acidus) are applied directly to the caruncle on several different occasions. A relative degree of symptomatic relief has been derived from such treatment, which is palliative in nature as pointed out by Meaker. Further or future treatment is based on recurrence of symptoms or recurrence of the tumor. Soothing salves and ointments have afforded relief in some cases.

b. Radium or roentgen therapy or the two together have many champions. Meaker stated that radium therapy has many successes to its credit but emphasized that burns should be avoided by the use of protective screens made of silver, brass, and rubber. He stated that a small dosage of radium, such as 25 to 30 milligrams applied for 2 to 6 hours according to the size of the tumor, is adequate. Loucks advised the same.

Quigley reported that radium therapy had been used in 25 cases with 1 to 16 year cures and that this is the specific treatment for urethral caruncles.

Radical treatment. a. Most authorities agree that simple fulguration—that is, destruction of the caruncle by the use of the electric current—accomplishes little more than the local application of caustics because it is superficial in extent and thereby encourages recurrence. Levant, however, advocated the monopolar type of current for fulguration which he used if the caruncle was telangiectatic and for desiccation if the lesion was papillomatous or granulomatous. He stated that this method has the advantages that it requires only a short time and that there is no possibility of hemorrhage, no possibility of infection, no scar tissue, freedom from postoperative symptoms, rapid relief, and no need of hospitalization.

Ballinger and Elder used the d'Arsonval high frequency current until all of the red growth was whitened.

b. Simple excision of the caruncles with the scalpel or scissors has led to a high incidence of recurrence and has been abandoned as a complete procedure in itself.

c. Excision with an electrosurgical knife or electric cutting loop or electric needle is advocated by some. Gutierrez advised the removal of caruncles by electrosurgical resection, cutting, and coagulating step by step. He used the following plan: procaine hydrochloride is injected at four points around the lesion; the tumor is removed with an electric knife; coagulation of the wound is carried out with the electric needle for hemostasis. No hospitalization is necessary.

Walther used a similar procedure which he described as follows: overdilatation of the urethra with a Kelly cone dilator or meatotomy is carried out; a traction suture is placed through the base of the tumor; the electric cautery is brought firmly in contact with the base of the lesion; bleeding is controlled by a coagulating current.

Stevens advocated a similar procedure with close follow-up and dilatation of the urethra at intervals to prevent formation of stricture.

d. Urethroplasty is the method of treatment accepted by many surgeons. All of the procedures and modifications will not be described. Deming described a well rounded procedure. He emphasized that the roots and ramifications of the tumor have to be destroyed to prevent recurrence. He advocated the following routine with the patient under general anesthesia: cuff excision is performed—that is, an incision is made through the mucous membrane around the external meatus; the mucous membrane of the urethra is then separated from the muscular layer for a sufficient distance beyond the tumor; a dorsal slit is made; a suture is placed in the dorsal region and the dissected mucosa is removed; the remaining urethral mucosal edge is sutured to the vaginal mucous membrane. Urethral catheterization is unnecessary. Deming reported complete relief by this method in 8 cases for periods ranging from 14 to 41 months.

Dodson advocated the foregoing procedure for the sessile type of caruncle.

Combination of conservative and radical methods. a. Simple excision plus caustic or cautery is one such combination. Kickham used a semicircular incision around the caruncle wide enough to include it and deep enough to include the full thickness of the mucous membrane. The caruncle is then excised and the base coagulated with a fine tip cautery. No sutures are necessary.

The Crenshaw method of treatment is carried out as follows (also described by Bumpus and associates):

1. The patient is placed in the lithotomy position, and the parts are thoroughly cleansed with soap and water. A swab of cotton on a toothpick saturated in 10 per cent solution of cocaine and lubricated with a soluble lubricant is inserted into the urethra and left for 10 minutes.

2. The labia are separated by an assistant. On examination the caruncle is found to consist either of a single tag on the posterior wall or of posterior or lateral masses. Each tag is picked up with a small Graefe fixation forceps and clamped off in the long axis of the urethra with a special clamp which has a broad blade and a narrow crushing edge. Care is taken to include in the bite all of the caruncle and none of the submucosal structure of the urethra.

3. The growth is cut off close to the upper surface of the clamp; the crushing of the pedicle prevents all bleeding and makes an accurate removal possible. *The specimen is saved for microscopic study.*

4. The cut surface is thoroughly seared with acid nitrate of mercury solution applied with a wooden applicator. An excess of the acid to run over the blades of the clamp and cauterize other areas of the urethral mucosa is cautiously avoided.

Crenshaw reported that in 118 cases there were only four recurrences.

According to Ferrier, the Crenshaw method, as described in the preceding paragraphs, is very satisfactory for all but the broadly sessile type. As a modification of this method he advised that, if the tumor is sessile, it be held with more than one fixation forceps in order to draw it all into the clamp, and further, in order to avoid the uncertain control of the acid caustic, that one use a small electrocautery such as is used by nose and throat surgeons, the cut edge being seared exactly as in the clamp and cautery operation for rectal hemorrhoids. He advocated the use of infiltration anesthesia.

Everett advocated similar treatment but always warned the patient about the great tendency of urethral caruncles to recur.

b. Excision and radium or roentgen therapy is another combination of conservative and radical treatment. Walther and Willoughby advised that one use the radiocutting loop to remove the caruncle and then follow up this procedure with radium or roentgen therapy.

HISTOPATHOLOGIC AND CLINICAL STUDY OF 120 CASES FROM THE MAYO CLINIC

One hundred and twenty cases of urethral caruncle were taken at random, those in which suitable gross specimens were available being given preference. Multiple sections were made from each specimen and stained with hematoxylin and eosin stain for microscopic study. The case records were studied, special attention being given to genitourinary symptoms and findings, treatment, and revisits. Follow-up letters were written to all patients requesting information as to their general health, symptoms referable to the genitourinary tract, and further treatment for previous trouble with the urethra. The microscopic sections were studied and an attempt was made to correlate these findings with the clinical symptoms, rate of recurrence, and age incidence.

The microscopic study included a thorough examination of the surface epithelium, the vascular reaction, and the cellular structure. The surface epithelium was found to be of the stratified squamous type in the majority of cases. However, transitional epithelium was present in some. Ulceration of the epithelial covering was most evident in the cases of chronic caruncle and in those in which there had been previous treatment with caustics, and so forth. Small islands of surface epithelium were found throughout the sections owing to the normal infolding of the urethral mucosa as described in the first part of this paper. The vascularity of the female urethra as described previously is abundant. The vascular reaction in these cases varied from simple dilatation to extravasation and actual thrombosis. This accounts for the red, angry appearance of this lesion, which is present in almost every patient. The uniformity of cell structure and lack of nuclear activity is evident (Figs. 1 through 4) and leaves little doubt as to the benign nature of urethral caruncles. The epithelial inclusions and urethral glands were studied closely and a few of the typical sections are included in this paper. The cell structure of the base of these lesions did not reveal the so-called "roots" or "ramifications" which have been described. In all

Fig. 1. Regional prolapse showing squamous epithelial covering, epithelial cell nests, dilated vessels, and lymphocytes (hematoxylin and eosin×55).

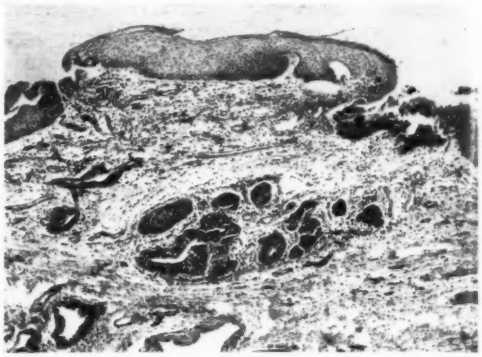

Fig. 2. Photomicrograph of section of caruncle showing glandular elements and epithelial nests (hematoxylin and eosin×30).

of the cases the initial change appeared to be a varying degree of prolapse of the urethral mucosa. This was regional in most instances, but was circumferential in others.

Of the 120 cases studied, 17 were asymptomatic. The microscopic picture in these cases was found to be the same as in the other 103 cases. The clinical picture was compared with the pathologic picture and no correlation was found. The cases with the most marked symptoms did not necessarily show the most marked pathologic changes. Only minimal changes were evident in some of the cases with severe symptoms.

The pedunculated appearance of some caruncles was explained on the basis of regional prolapse encouraged by the crypts and infoldings of the urethral mucosa. This appearance was further accentuated when irritation due to clothing, pads, and so forth took place, leading to vascular congestion.

From the material studied for the preparation of this paper, it is our impression that urethral caruncles are due to several factors. Among these are the anatomic structure of the female urethra, which encourages regional as well as circumscribed prolapse; the anatomic location of the urethral meatus, resulting in almost constant exposure to trauma and irritation; and the histologic structure, which encourages marked inflammation and congestion as well as increased sensitivity. For these reasons the caruncle may be symptomatic or asymptomatic, be localized or circumscribed, and occur in young as well as old people.

The symptoms of the urethral caruncle may vary from none at all to those of extreme severity. This wide variation cannot be explained on the basis of the gross or microscopic appearance. In this series of cases the signs or symptoms complained of most frequently were pain while sitting, walking, during intercourse, and so forth; smarting on urination; bleeding from the genital region; tumor mass in genital region; and frequency of urination. The patients complained of any one or all of these symptoms. Several of the patients had no symptoms, the caruncle being discovered on routine examination of the genital region. The size and location of the caruncle had no bearing on the severity of the symptoms. Their duration varied from 10 days to 17 years.

In our series the greatest number of urethral caruncles was encountered between the ages of 40 and 70 years. However, the age range extended from 6 to 88 years, the postmenopausal and multipara accounting for the majority. Of the premenopausal patients 65 per cent had children; of the postmenopausal patients 54 per cent had children. The age of the patient had nothing to do with the severity of the symptoms. As shown in the review of the literature, much emphasis has been placed on the age and marital history as etiologic factors. We believe that these are contributing factors and not basically etiologic.

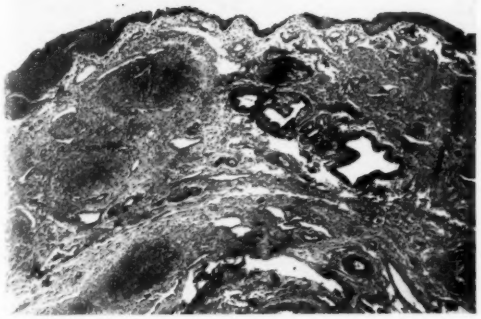

Fig. 3. Section of circumferential prolapse showing same findings as Figure 2 (hematoxylin and eosin×30).

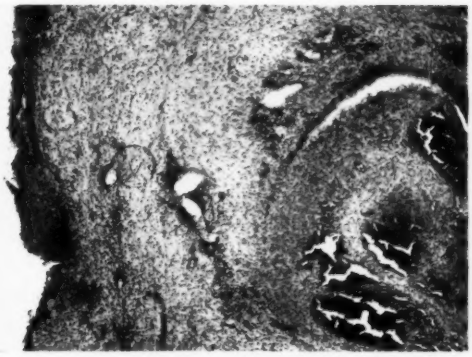

Fig. 4. Region of thrombosis in a caruncle (hematoxylin and eosin×20).

The different types, as described in the literature, were seen in this series but regardless of the classification used, the basis is still the same—varying degrees of urethral prolapse and irritative reaction. By having so many different classifications one is complicating the picture and encouraging continued confusion. Urethral caruncle and urethral prolapse should be included under the same major heading, "urethral prolapse." We are not advocating the discontinuance of use of the term "urethral caruncle," for this term has a definite place in medical literature through its long usage. It could be applied to that group of urethral prolapses which is localized, whether sessile or pedunculated, in contradistinction to the circumscribed or circumferential type of prolapse.

It is evident that the most important differential diagnostic point is obtained by microscopic study of the pathologic specimens. This fact cannot be overemphasized, for the ultimate diagnosis depends on this alone. One should not forget that the urethral caruncle and malignant lesions of the urethra can and do coexist.

Treatment. What is the correct treatment for urethral caruncle? This question cannot be answered in this paper and the current literature helps very little. The more one reads the more confused one becomes, because there are so many methods and modifications offered. No one treatment is acceptable or applicable in all cases. The incidence of recurrence is high if the patients are followed long and closely enough. Classic is Ferrier's statement that few lesions of such distressing symptoms have been treated so unsurgically by surgeons.

In this series of 120 cases nearly two-thirds of the patients who answered follow-up letters had recurrences of the caruncle regardless of the method used. The number of recurrences varied from 1 to 9. With this high rate of recurrence, the patient should be warned that recurrence is extremely likely and that further treatment may be necessary. The main purpose of the treatment offered is symptomatic relief. This should be secured by the simplest and most suitable treatment, depending on the nature of the lesion. The treatment should be carried out as an office procedure if possible; a specimen should be preserved for pathologic study; stricture formation should be made unlikely by following treatment with periodic urethral dilatation; and the treatment should be of such a nature that it can be repeated again and again, if the lesion does recur, without danger of complication.

The objection to the more radical procedures, such as urethroplasty, is that if they are not performed by a competent surgeon, the urethra may be so shortened at the initial or subsequent operation as to result in urinary incontinence. This is encountered most commonly in the treatment of the circumferential type of prolapse where the urethra is actually shortened or the ureteral orifices pulled down into the urethra.

Most of the various methods of treatment were described in the first part of this paper. This was done because we feel that all of them may have a place in the treatment of urethral caruncle. No one type will successfully care for all of the various degrees of prolapse; each may have its own place and indications. We feel that complete removal is advisable but do not believe that so much emphasis should be placed on destruction of the so-called roots of the caruncle.

CONCLUSIONS

On the basis of a complete review of the literature and review of 120 cases, including follow up of patients and study of microscopic sections of pathologic specimens, the following conclusions are drawn:

1. The anatomic and histologic structure of the female urethra encourages regional or circumscribed prolapse. The prolapse may be internal or external to the urethral meatus.

2. The varying degrees of trauma, irritation, and so forth to which this prolapsed mucosa is subjected give rise to varied microscopic pictures.

3. Examination of cross sections through the urethral glands and mucosal infoldings has led to the misdiagnosis of neoplasm or precancerous lesion. Urethral caruncle is definitely a benign lesion, but may coexist with carcinoma of the urethra.

4. The treatment offered is only palliative and rarely curative. The incidence of recurrence is high and further treatment is often required.

5. Regional or circumscribed urethral mucosal prolapse or both would be the only hypothesis which could explain the occurrence of urethral caruncle in all ages and the varied symptomatic pictures, ranging from no symptoms to most severe symptoms.

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A CRITIQUE OF THE McVAY OPERATION FOR INGUINAL HERNIA

THE continued search for improved methods for the repair of inguinal hernia is a laudable effort. New techniques should be critically investigated, and if they appear to be logically conceived, should be given adequate trial. Many innovations will fall by the wayside. A recent suggestion has been the reintroduction by McVay of the utilization of Cooper's ligament in inguinal herniorrhaphy. This method has been enthusiastically received in a number of clinics, and excellent results are reported with it. However, there are certain fallacies apparent in the approach to this method, which should receive mention.

On the basis of an excellent study of the inguinofemoral anatomy conducted in conjunction with Dr. Anson at Northwestern University, McVay[1] concluded that the "fundamental error" in current methods of inguinal herniorrhaphy is the utilization of the inguinal ligament as the bastion to which the muscles and fascia of the abdominal wall are sutured. He correctly pointed out that, instead of being a fixed structure, as is usually conceived, the inguinal ligament is mobile, being firmly anchored only at its two extremities. During the remainder of its course it is attached to the fascia lata of the thigh by only the thin investing fascia of the external oblique. He found further that the transversalis fascia instead of inserting into the inguinal ligament, as is usually described, is only loosely connected with that structure and actually inserts into the superior pubic (Cooper's) ligament. On the basis of these findings, he expressed the conviction that the almost universal utilization of the inguinal ligament is a cardinal error in herniorrhaphy, and his recommendation was that the Cooper's ligament be used in its stead.

There are several objections to this point of view. To consider this the fundamental error in inguinal herniorrhaphy would imply that operations fail because of lack of fixity of the structure to which the abdominal strata are sutured. Were this so, the recurrences thereby brought about would be due to the inguinal ligament being drawn upward, with resultant defect below it, and recurrence in the femoral region. While this type of recurrence may occur, it is certainly very rare. As all descriptions of recurrent hernias testify, the overwhelming majority of recurrences take place above the inguinal ligament, at the site of the original defect. This being so, it is difficult to see how failure to utilize a firmer support could obviate these failures.

[1] McVAY, C. B., and ANSON, B. J. Surg. Gyn. Obst., 1942, 74: 746–750.

It is certainly true that the transversalis fascia inserts into the superior pubic ligament and that its attachment to the inguinal ligament is merely one of contiguity through the agency of the thin investing fascia of the transversus abdominis muscle and aponeurosis. Nevertheless, any suture placed in the inguinal ligament for the purpose of uniting the transversalis fascia to it must, of necessity, include the distal portions of the transversalis fascia, namely, those which extend from the inguinal to the superior pubic ligaments. Continuity of this aponeurotic layer is therefore restored by such sutures.

From a technical point of view, there are further objections to the Cooper's ligament technique. The operation is technically more difficult than are those utilizing the inguinal ligament, and the possibilities of injury to the femoral vein are vastly greater. While a surgeon of McVay's technical ability and extraordinary familiarity with the anatomical structures involved can unquestionably perform this operation with complete security, the same cannot be said of surgeons generally who are charged with the repair of inguinal hernias. Those who have attempted to utilize the superior pubic ligament in the repair of inguinal or femoral hernias, are aware of the greater difficulties of exposure. Drawings made from cadaver material in no way portray the problem experienced at the operating table by the bulging and protrusion of the preperitoneal fatty tissue which makes visualization of the superior pubic ramus extremely difficult. More important is the proximity of the femoral vein, so that direct trauma and secondary thrombosis must be expected in a much larger incidence than occur with inguinal ligament herniorrhaphies.

The femoral vessels interpose another difficulty. While it is true that the medial portion of the inguinal canal can be closed by suture of the transversalis fascia with or without internal oblique muscle to Cooper's ligament, the lateral portion of the canal cannot be so obliterated because of the presence of femoral vessels crossing the superior pubic ramus. This is the portion of the canal involved in indirect hernias, the most frequent of all hernial types. In order to close this portion of the canal, Harkins,[2] who has enthusiastically endorsed the McVay method, sutures the lateral portion of his fascias to the inguinal ligament. This step-like procedure does not lend itself to accurate closure, and the femoral vein itself forms part of the wall of the canal. McVay, however, uses a somewhat different method. He "carefully elevates the inguinal ligament so that the suture line incorporates only the anterior layer of the femoral sheath."[3]

One further theoretical consideration suggests itself. Any operation which is predicated upon the need of a firm and unyielding bastion to resist the pull of muscular structures must be wrong in its conception. If the sutures themselves are strong enough to resist this muscular pull, they will then cut through by the process of progressive ischemic necrosis of the tissues which are subjected to pressure against the suture material. As a fundamental requirement therefore in the surgical approach to any hernial repair, the technique must be planned to avoid tension and pull. Otherwise the operation itself is faulty in its philosophy, and no amount of strength of suture material or anchoring structure will compensate for what is a fundamental fallacy.

The criticisms detailed above do not in any way deny the correctness of McVay's anatomical observations, nor do they question the excellent results which have been obtained by the Cooper ligament technique. Furthermore

[2] HARKINS, H. N., and SCHUG, R. N. Arch. Surg., 1947, 55 689–709.
[3] MCVAY, C. B. Personal communication.

the rationale of using the superior pubic ligament in the repair of femoral hernias is obvious. They do, however, strongly doubt the assumption that lack of fixity of the inguinal ligament is the fundamental error in current operative techniques for inguinal hernia. And while results obtained may be as good as have been reported, it remains to be shown that equally favorable results could not have been secured with the utilization of the more accessible inguinal ligament. Whatever improvement in results may be claimed for the method must be balanced against the added difficulties and hazards which the McVay technique entails. Approached from this point of view, it appears scarcely credible that superior pubic ligament will replace the inguinal ligament in the routine repair of inguinal hernias.

LEO M. ZIMMERMAN.

THE DIAMOND JUBILEE OF PROFESSIONAL NURSING

LINDA RICHARDS, America's first "trained nurse" graduated in 1873, the year in which the "Nightingale system" of nursing education was established in three schools of nursing associated with hospitals in New York, Boston, and New Haven. The figure of Linda Richards has become symbolical of professional nursing in America. Able, and energetic, Miss Richards went to London soon after her graduation to confer with Miss Nightingale and to work in English and Scottish hospitals until she became familiar with the Nightingale principles of nursing education. Miss Richards established no less than ten schools of nursing during her lifetime: nine in the United States and one under missionary auspices in Japan. Her versatility was further demonstrated by her interest in the care of the insane and in the promotion of visiting nursing services.

For two reasons, the times were ripe for the development of nursing. First, women were seeking new opportunities outside of the home. Second, the use of anesthesia and the rise of bacteriological science were contributing to the rapid development of surgery. From that point on, nursing and surgery went forward hand in hand with a resultant rapid increase in the number of American hospitals.

The main principles of the so-called Nightingale system of nursing education were:

1. The nursing service of the hospital and the instruction of nursing students should be under the direction of a qualified nurse.

2. The school of nursing should have its own financial resources independent of the hospital which provided the clinical experience.

3. There should be a planned course of instruction making provision for both the preventive and curative aspects of nursing.

4. A suitable residence should be provided for the nursing students.

With one or two notable exceptions, the early American schools were soon absorbed by the hospitals, lost their identity as schools, and became administrative assets of the hospitals. As time went on, it became evident that the demands on American nurses required a broader preparation than that acquired through an apprenticeship in a hospital. Three important studies of nursing and nursing education have been made during the past quarter of a century.

In 1922, the Goldmark study, financed by the Rockefeller Foundation, pointed out the necessity for more extensive preparation for public health nurses. By 1925, there were more than 2,500 schools of nursing in the United States, many of them operated by hospitals of questionable quality. Lack of standards in these schools led to the organization of the "Grading Committee" on which the American College of Surgeons had mem-

bership. As a result of the nation-wide study made by this committee and aided fortuitously by the economic depression, the number of nursing schools was reduced to about 1,500. Unfortunately, the "Grading Committee" did not publish a list of schools indicating their rank or grade. Therefore, neither the prospective student nor the public was able to determine the quality of any particular school. Many nurses earned diplomas from schools of nursing only to find after graduation that the quality of their education made them ineligible for various types of nursing work.

The third study recently published by the Russell Sage Foundation and popularly known as the "Brown Study" was financed by the Carnegie Foundation and clearly points to the next stage in the evolution of American nursing.

One of the characteristics of American nursing has been its willingness to submit to critical self-analysis. The Diamond Jubilee of Professional Nursing gives us an opportunity to acquaint the public with the achievements of the nursing profession in America, and more importantly, it enables us to secure the interest and understanding of allied professions and the general public in the further adaptation of nursing service to the present and future needs of the American people.

PEARL MCIVER.

The National Portrait Gallery

SIR CHRISTOPHER WREN, F. R. S.

After the portrait by Sir Godfrey Kneller, painted in 1711.

THE SURGEON'S LIBRARY

THE BOOK SHELF

DOCTOR THOMAS WILLIS AND SIR CHRISTOPHER WREN

BARRY J. ANSON, Ph.D. (Med. Sci.), Chicago, Illinois

IN the entire course of the history of medicine there is no more illustrious association of author and artist than that represented by the collaborative effort of Willis and Wren in the preparation of *Cerebri Anatome Nervorumque Descriptie et Usus* (1664).[1] Each, eminent in his profession, brought to this conjoint endeavor an ability exceeding that of contemporary writers and craftsmen. While their contributions to the treatise might have seemed, at the time, equal in value, a present day appraisal of worth would, in respect to accuracy, tip the balance in favor of Sir Christopher: his delineations of neural morphology are so faithful to the dissected subjects that they might be of laboratory service today; the interpretive text by Doctor Willis (Fig. 1), on the contrary, is a repository for an outmoded concept of bodily activity. The illustrator's path was straightforward; he prepared pictorial records of observed anatomic features. The author's approach to his task was, of necessity, oblique; his thinking was deflected from a straight course, among morphological landmarks, by potent doctrinal winds of Graeco-Roman origin. He must translate mystery as he undertook "to explicate the uses of the brain." To Doctor Willis this seemed "as difficult a task as to paint the soul, of which it is commonly said that it understands all things but its self." To the nature of their diverse accomplishments we shall return, after having reviewed certain important biographical facts.

Thomas Willis began his study of medicine at Oxford in 1642. In that year, besieged by the armies of Parliament, King Charles retired to Oxford, which he proceeded to fortify. Willis, faithful to the King, was a member of the defending garrison. Among the notable men in Oxford at the time, was William Harvey, the King's favorite physician. Thomas Willis graduated a Bachelor of Medicine in December, 1646. In the same year Harvey left the service of the King and returned to London. Thomas Willis remained in Oxford, as a practitioner of medicine. With the restoration of Charles II in 1660, Willis' loyalty was rewarded; he was made Sedlies Professor of Natural Philosophy.[2]

In 1645, before the civil war had reached its conclusion, a group of scholarly Londoners organized themselves into a society "for inquiry into natural philosophy." By their removal to Oxford in 1648, the society became divided; however, they were united and chartered in 1662 by the King as the Royal Society of London. Thomas Willis was elected a Fellow of the Society in 1663.

In his scientific endeavors, Thomas Willis was beholden to Richard Lower and Christopher Wren, and he acknowledges the bond of gratitude in his preface to *The Anatomy of the Brain:* "for the more accurate performing of this work," Willis writes, "I made use of the labours of the most learned physician and highly skillful anatomist, Dr. Richard Lower, for my help and companion; the edge of whose knife and wit I willingly acknowledge to have been an help for the better searching out both the frame and offices of before hidden bodies." To Christopher Wren, Willis expresses his indebtedness for the delineation of the "many figures of the brain and skull" (Figs. 2a to 2d).

Richard Lower was a physician of London, and author of a treatise on the anatomy of the heart, *Tractatus de Corde*, published in 1669. Lower knew that the movement of the blood depended upon that of the heart; he described minutely the whorly course of the cardiac fibers, and their of-

Contribution No. 496 from the Department of Anatomy, Northwestern University Medical School.

[1]Thomas Willis' original account was published in 1664. Later it appeared as part of a volume of eleven treatises. The combined work is the *Practice of Physick*, published in London in 1684. The treatise on the brain (Number VI of the series) is hereinafter employed as source of quoted passages and of figures. It is the fourth in the *Five Treatises* published in London in 1681.

[2]Notes from *Thomas Willis*, by William Snow Miller, *Bulletin of the Society of Medical History of Chicago*, vol. 3, no. 2, Oct. 1923, pp. 215-232.

fice in contraction of the muscular walls; he recognized the correlation between ventricular thickness and muscular effort in systolic contraction; he described and figured the venous valves, and accounted for their function. Lower not only elaborated clearly and serviceably upon Harvey's concept of the circulation, but stated that "whatever statements writers before Harvey made about the movement of the blood through the ventricles of the heart are so empty and worthless that they have already spontaneously disappeared into oblivion." As will be seen, however, it was Richard Lower's teacher and friend, Thomas Willis, who managed to pluck the outworn notion from oblivious fate.

In his early years Christopher Wren (frontispiece) occupied himself chiefly with astronomical and mathematical studies, and with invention. Following the outbreak of the Great Plague, in 1665, he left London, for a visit to Paris.[3] At the end of 6 months, in February of the year 1666, he was summoned back to England, to report on the repair of Old St. Paul's. While so engaged he regularly attended the meetings of the Royal Society, then mainly engaged in considering how a return of the pest could be averted. In September of the same year came the Great Fire, and the City of London was destroyed. With energetic alertness, Wren submitted to the King his design for the rebuilding of the City. In response, his monarch appointed Wren the Surveyor-General, a post which he held for almost half a century. In this capacity, he became architect for "repairing the whole City, the Cathedral Church of St. Paul's, all the parochial churches with other public structures." Certain of these assignments were of monumental proportions—the rebuilding of the dome of St. Paul's Cathedral occupying at least part of his attention for forty years. Additionally, he is credited with the rebuilding of some fifty-two London churches (Fig. 3).

Christopher Wren's early education was mainly scientific. Not only was he a regular attendant at meetings of the Royal Society, but also one of its founders and later its President (in 1680). He was a member of Parliament, a shareholder in the Hudson Bay Company during the period of England's territorial expansion, and a public-spirited Londoner, who was consulted on all matters connected with the City—unremittingly aidful, to his death at ninety-one years of age.

Before Christopher Wren became an architect he was already a scientist of European fame, a compeer of Harvey and Newton. His genius was displayed not only in the fields of mathematics, astronomy, and invention, but also in some departments of medicine. He came to occupy the chair of Astronomy at Gresham College in London at the age of twenty-five; three years later he was appointed Savill Professor at Oxford. With the genius of a Leonardo, he invented, or proposed plans for, a weather-clock, an artificial eye with humoral content, an instrument for writing double, new ways of engraving and etching and methods of submarine navigation. He introduced liquids into the blood stream of animals, forecasting similar experimental practice in transfusion and in hypodermic injection. In the field of physiological experimentation there is, curiously, no reconciliation between his own observations and the physiological notions held by Willis—as there is none between theirs and the concepts of Harvey and Lower. Despite the fact that they were colleagues and fellow-members of the Royal Society, their anatomic views seem insulated possessions —individualistically held, and never reconcilable contributions to an accumulated store.

Sir Christopher Wren's figures of the brain (Figs. 2a to 2d) take their place in a large gallery of neurological illustrations (Figs. 4a to 4f, 5a to 5f).[4] Predecessor, pre-Vesalian, figures are those of Albertus Magnus, Johannes Peyligk, Gregor Reisch, Wendelin Hock, and Johann Dryander; those encountered in the magnificent *Fabrica* of Vesalius, and in the contemporary volumes by Charles Estienne, Constanzio Varolio and Bartolommeo Eustachi; in the later treatises by Caspar Bartholin, Johann Vesling, Raymond de Vieussens, Godfried Bidloo and Giovanni Domenico Santorini—and all these antecedent to the first editions of textbooks of gross anatomy and neuroanatomy. Wren's drawings are less delicate than those of Santorini, less forceful than the neurological figures in the Vesalian *Fabrica;* they are far more attractive than the contemporary illustrations in the *Syntagma* of Vesling, in the *Neurographia* of Vieussens, and in the *Institutiones* of Bartholin; they are more analytical, though far less statuesque, than the comparable figures in the folio volume of Bidloo.

In order to appreciate fully the degree to which Willis' system is dependent upon the primitive

[3]Biographical notes from *Sir Christopher Wren*, Bicentenary Memorial Volume published under the auspices of the Royal Institute of British Architects. Hodder and Stoughton, London, 1923.

[4]In these two plates of illustrations all but figures 4a to 4c and 5a were photographed from the original volumes, in the Archibald Church Library of Northwestern University Medical School.

Figures 4e and 4f were copied from the *Opera Omnia Anatomica et Chirurgia* of Boerhaave and Albinus, which is the 1725 revision of Andreas Vesalius' *De Humani Corporis Fabrica Libri Septem.* In the edition of 1725 the figures were reproduced from copper engravings. It will be remembered that the three editions (1543, 1555, 1568) of the *Fabrica* published during the life of Vesalius contain wood-cuts, again used in the German edition (1783) by Leveling.

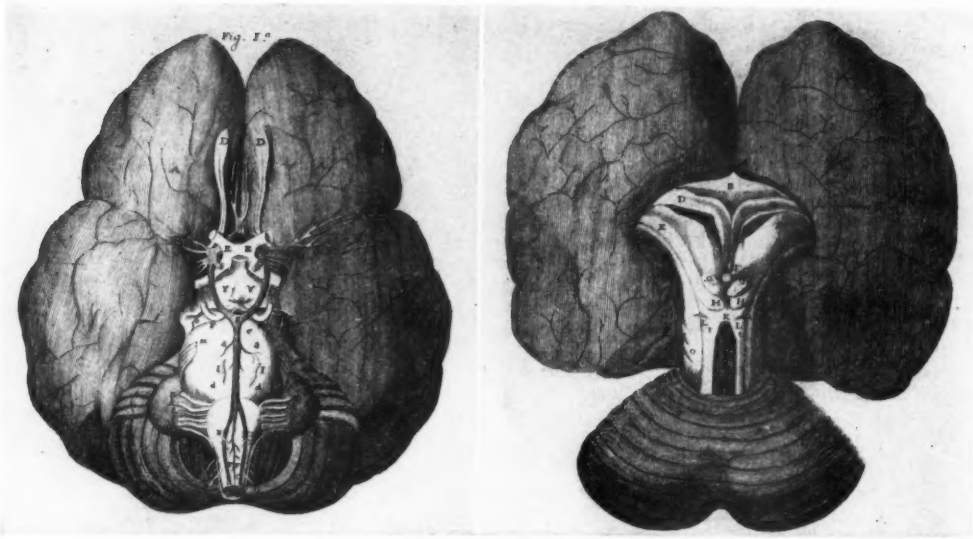
writings in the medical sciences, it is necessary to examine more than his accounts of the heart and of the brain. The essential elements are continued in the *Practice of Physick*, published in 1684 (Fig. 6). Herein the reader is presented with an inclusive picture of medical concepts which are negligibly influenced by William Harvey's account of the nature and the circuiar movement of the blood. More than a half century after the publication of Harvey's treatise, and fifteen years after the appearance of Richard Lower's tract on the heart, Willis' concept of nervous physiology was still based upon the Galenic notion of vapors and distillates—a system which then was fifteen hundred years old.

Thomas Willis, eschewing the knowledge recorded in the works of Harvey and Lower, clings to the ancient doctrine of the spiritus or pneuma, perpetuating the traditional belief that the body of man is an anthropomorphous sponge designed to house a leavening breath of celestial origin. Air, with its burden of spiritus, was thought to be inhaled and vented through the trachea and the innumerable cutaneous pores, the latter openings being described as if they were the peripheral ostia of the blood vessels. Alimentary fuel for the bodily fire was carried by the portal vein to the liver; in the liver this nutrient chyle transformed into the natural spirit, whose function it was to control nutrition, growth, and reproduction. The heart drew this nutritive mixture from the hepatic pulp to its own right chamber, wherefrom it was wafted through the interventricular wall—supposedly porous—to attain the left ventricular chamber. Mixed with the inhaled breath, the natural spirit was converted into the vital. The greater part of this vaporous compound was believed to be carried away by the arteries to serve as the source of life and the bodily heat. However, a small part of this life-giving spirit was admitted to the complex arterial network at the base of the brain. In this miraculous plexus, termed the *rete mirabile*, the spiritus was rendered fit to perform the animal functions, that is, to impart sense and to cause motion. In this thrice refined form, the spiritus lingered within the brain as the substance of opinion and judgment and the stuff of the human soul.

Doctor Thomas Willis modernized this early philosophic doctrine by bringing to the Galenic notion of pneumatic elaboration that of fermentive inkindling. Willis believed that fermentation is not limited to the formation of yeast, to the souring of vinegar, and to other ordinary zymic processes, but that it is an all pervasive chemical phenomenon which accounts as well for the normal heating of the human blood and for its uncontrolled intensity in fevers. Willis believed that the process of distillation was as essential in bodily metabolism as it was fundamental to the preparation of healing pharmaceuticals. Distillation served as a means of separating volatile materials from substance of more fixed character. In simple form the apparatus consisted of a gourd-shaped cucurbite, a shrouding alembic cemented to the former, a stove and a receiver (Fig. 7). The substances were macerated and digested in the heated cucurbite; the vapors, condensed in the alembic, were carried away through the beak of the alembic to the receiver.[5] As will be seen, Willis found the counterparts of these distillatory pieces in the human thorax and head. To him, the calvarium, together with the subjacent meninges and brain, was a kind of alembic; the heart

Fig. 1. Portrait of Thomas Willis, Sidley Professor of Natural Philosophy at Oxford.

[5]Comments from *Pictoria History of Ancient Pharmacy, with Sketches of Early Medical Practice*, by Hermann Peters, transl., Wm. Netter, G. P. Englehard, Chicago, 1889.



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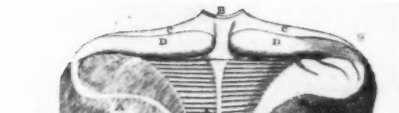

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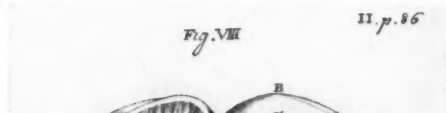


d

Fig. 2. Figures II, III, VII and VIII from *The Anatomy of the Brain* in the *Practice of Physick* by Thomas Willis (1684). a, "The basis tof a sheep brain taken out of the skull, and the roots of the vessels cut off, where all the arteries, by ink being injected into one of the carotides, are made black and more conspicuous." b, Showing "the outmost or superior superficies of the humane brain taken out of the skull; where the border of the brain being loosened from the knitting of the other parts, made by the membranes, is elevated and turned outward, that the shanks of

(*Legend continued on opposite page*)

Fig. 3. Sir Christopher Wren's principal buildings in London and elsewhere. Drawing by C. R. Cockerell, R.A., engraved by Wm. Richardson. From *Sir Christopher Wren*, Bicentenary Memorial Volume published under the auspices of the Royal Institute of British Architects, Hodder and Stoughton, London, 1923.

and its great vessels behaved as the cucurbite and the distilling stove (Fig. 8).

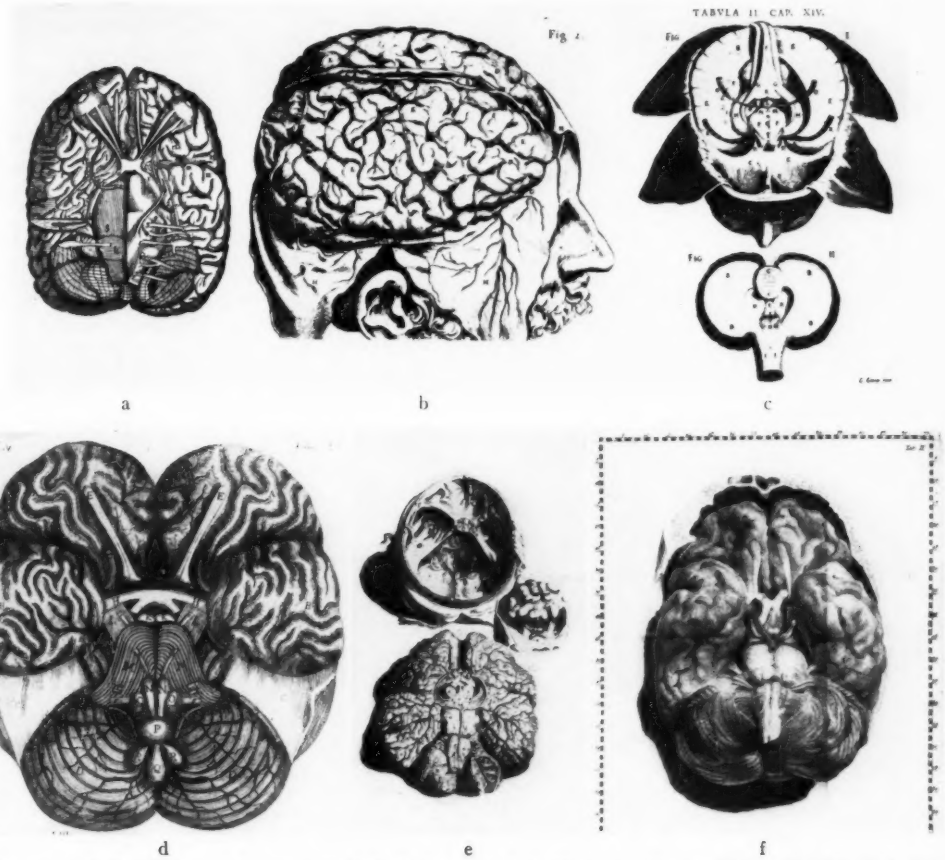
Although he retained the ancient distillery as part of the physiological machinery, Willis, influenced by the then new chemistry, could no longer regard the spiritus as a self-sufficient vapor intermediate between body and soul; he must think of it in association with sulphur, niter and salt. In his system, heavenly spirit became an alloy through fermentive interaction with mundane elements. Regarding the spiritous part of the compound, Willis writes that its constituents are highly subtle, "Aetherial Particles of a more Divine Breathing, which our Parent Nature hath hid in this Sublunary World, as it were the Instruments of Life and Soul, of Motion and Sense." Being volatile, they are always "endeavouring to fly away"; consequently, "lest they should too soon leave their subjects, they are bound sometimes with more thick Particles." Through the process of fermentation, operative within the chambers of the heart and its major vessels, the particles of the four elements, freshly ebullient, "like Water boyling over a Fire," the blood is propulsed through the vascular channels, "not without great Tumult and Turgescency." The degree of admixture makes a chemical hierarchy, with the motionless minerals, of fixed nature, at one end of the scale, and living creatures at the other —the animate things being rich in spirit, as would be requisite for sense and motion.

Willis would extend this concept to account for the final elaboration of animal spirit in the brain. This is the textual and pictorial burden of the *Cerebri Anatome*. Doctor Willis ventures the guess "that the Brain with Scull over it, and the appending Nerves, represent the Little Head or Glassie Alembic a Spunge laid upon it, as we use to do for the highly rectifying of the Spirit of Wine." The blood, rarefied by the cardiac heat, is carried from "the Chimny of the Heart, to the

the oblong marrow, the fornix or arched vault . . . and other processes, may be clearly and distinctly beheld." c, "The brain of a sheep bent back and cut a little open in the places where they stick together near the streaked bodies, that its interior substance may be turned the inside out, and unfolded on a plain." d, "Represents the oblong marrow taken out of the head of a sheep with the brain cut off and removed, and with the cerebel and one streaked body cut in two in the middle, and other things chiefly belonging to the medullar trunk."

Figs. 4a to 4f. The anatomy of the brain; illustrations from classical sources. a, Johannes Peyligk: *Philosophie Naturalis Compendium*, 1490. b, Albertus Magnus: *Philosophia Naturalis*, 1506. c, Johann Dryander (Eichmann): *Anatomia Pars Prior*, 1537. d, Bartolommeo Eustachi: *Tabulae Anatomicae*, 1769. e and f, Boerhaave and Albinus: *Opera Omnia* (1725 revision of *De Humani Corporis Fabrica Libri Septum* by Andreas Vesalius).

Head, even as the Spirit of Wine Boyling in the Cucurbit, and being resolved into Vapour, is elevated into the Alembick"; the latter "only transmits or suffers to pass through the more penetrating and very subtil Spirits, and carries them to the spout of the Alembick; in the mean time, the more thick Particles, are strayed, and hindred from passing." In this manner, "the blood being delated into the Head, its spirituous, volatil, and subtil Particles, being restrained within by the Skull, and its menynges, as by an Alembick, are drunk up by the spungy substance of the Brain, and there being made more noble or excellent, are derived into the Nerves, as so many spouts hanging to it." The crass, or thick, particles of the blood, being hindered from entering the brain, are carried back by the circulation to the heart for further rectification. In the cerebral substance the spirituous and most subtle portion, being as it were distilled from the blood, undergoes final purification; there, being "inspired by a certain Ferment, whereby it is yet more volatilised, it is made

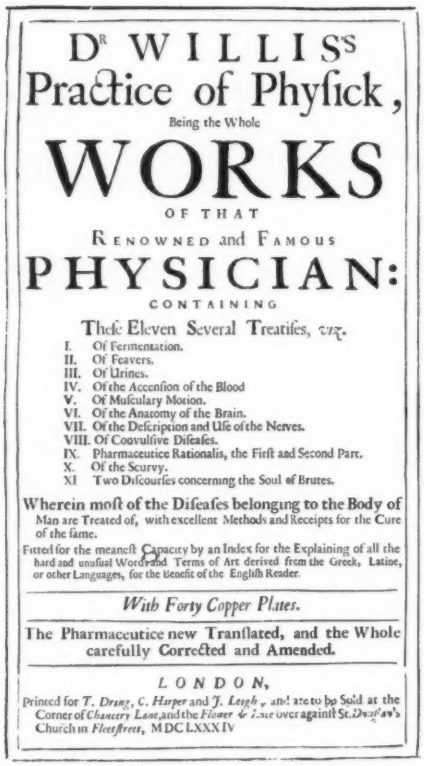


Figs. 5a to 5f. Illustrations of the anatomy of the brain continued. a, Constanzio Varolio: *De Nervis Opticis*, 1573. b, Caspar Bartholin: *Institutiones Anatomicae*, 1641. c, Johann Vesling: *Syntagma Anatomicum*, 1647. d, Raymond de Vieussens: *Neurographia Universalis*, 1685. e, Godfried Bidloo: *Anatomia Humani Corporis*, 1685. f, Giovanni Domenico Santorini: *Septem Decim Tabulae*, 1775.

more fit for the performing the offices of motion and sense"; to this end "the substance of the Brain is exceeding full of a Volatile Salt, which is of great Virtue for the sharpning and subtilising the spirits."

In the treatise entitled "Of the Accension of the Blood," Thomas Willis discusses particularly the "growing hot or inkindling of the Blood" (Fig. 6). In order that a flame may be inkindled in the heart and continue to burn "there is need of a free and undiscontinued access of Air"; to this end the action of the lungs serves to carry away "the vaporous Effluvia's, threatening the suffocation of the flame," and to supply "nitrous food necessarily requisite for the burning." Like a flame, the life of the blood may require additional ventilation; "to which end, besides the greater breathing places of the Breast, innumerable lesser, *viz.* the Pores of the skin gaping everywhere through the whole Body, do send forth Effluvia's departing plentifully from the boiling blood." If alimentary fuel for the cardiac fire be denied, the vigor of the blood is diminished; and when the nutriment becomes "too thin and watry, the fervour of the blood, like flame without food, uses to be remitted."

Recognizing that the flame inkindled in the blood "appears not at all," Willis records his belief that "it is most thin, and burns in the Heart,



D^R WILLIS^S
Practice of Phyſick,
Being the Whole
WORKS
OF THAT
RENOWNED and FAMOUS
PHYSICIAN:
CONTAINING
Theſe Eleven Several Treatiſes, viz.
I. Of Fermentation.
II. Of Feavers.
III. Of Urines.
IV. Of the Accenſion of the Blood
V. Of Muſculary Motion.
VI. Of the Anatomy of the Brain.
VII. Of the Deſcription and Uſe of the Nerves.
VIII. Of Convulſive Diſeaſes.
IX. Pharmaceutice Rationalis, the Firſt and Second Part.
X. Of the Scurvy.
XI Two Diſcourſes concerning the Soul of Brutes.
Wherein moſt of the Diſeaſes belonging to the Body of Man are Treated of, with excellent Methods and Receipts for the Cure of the ſame.
Fitted for the meaneſt Capacity by an Index for the Explaining of all the hard and unuſual Words and Terms of Art derived from the Greek, Latine, or other Languages, for the Benefit of the Engliſh Reader.
With Forty Copper Plates.
The Pharmaceutice new Tranſlated, and the Whole carefully Corrected and Amended.
LONDON,
Printed for *T. Dring, C. Harper* and *J. Leigh*, and are to be Sold at the Corner of *Chancery Lane*, and the *Flower de Luce* over againſt St. *Dunſtan's* Church in *Fleetſtreet*, MDCLXXXIV

Fig. 6. Title page of Thomas Willis' *Practice of Physick* (1684).

and its depending Vessels as it were shut up in Receptacles"; it does not blaze clearly, "but perhaps remains in the form of smoke, or a vapour, or breath"; even should the blood "openly flame out, yet it might be so done, that its shining being most thin, may not be perceived by our sight, as in the clear light of the day we cannot behold a glowing red-hot iron, nor shining sparks, nor false fires, nor rotten wood, nor many things shining by night."[6]

[6]Willis finds support for his opinion in the fact that some "hot living Creatures . . . send forth a certain fire or vaporous blood, when they have put off their inner garments at night going to bed near a fire or Candle." Similarly, it is noticed "in a burning Feaver, caused by immoderate drinking of Wine or strong Waters, that the blood, as the flame of it is very much increased, doth grow excessively hot," even to the degree that some believe they have seen the "burning fires and flame in the eyes"; these observations argue "that the blood is very strong, and also that it penetrates the inclosure of the Brain." Willis himself knew "a certain ingenious Man of a very hot brain, who affirmed, that after a very plentiful drinking of Wine, he was able in the darkest night to read clearly."

In accounting for the further movement of the heated spiritus, the arteries, veins, venous sinuses of the dura, cerebral ventricles, cerebrum, cerebellum and medulla oblongata are all brought logically, but erroneously, into the traditional physiological scheme; each gross anatomical part is employed as if it were a living sieve, retort or pipe in a neurological distillery. When it is received from the heart, the spiritus finds its loftiest residence in the brain. In this final anatomical station, it is fully elaborated, preparatory to carriage by spinal and peripheral portions of the nervous system to the muscles and to the organs of sense.

The large vessels, carotid and vertebral, are the major conduits from the heart to the brain; either pair of these "inclining one towards the other are mutually conjoyned." Correspondingly, the meninges are "stuffed throughout with veins, sent from four bosoms" (the dural sinuses of our description) which ultimately receive the blood from the anastomosis of arteries now termed the *circulus arteriosus Willisi* (Fig. 2a). The veins "like promptuaries or store houses framed in several places," are destined to receive the blood "returning from every region and corner of the brain," and "at length transfer their burden into the jugular veins."

The globous brain is aptly described as being marked externally by chinks, "turning and winding like to the rollings about of the intestines." Upon removal of the cerebral hemispheres there is exposed an internal substance, which, throughout its extent, is "chamfered or streaked." In Willis' opinion these markings "were made by nature, as it were passages or channels for the passage and return, or going to or from of the spirits out of the callous body into the oblong marrow, and on the contrary" (Fig. 2b). That is to say, cerebral substance is physiologically important in so far as it is a spongious or a foraminous mass fit to transmit the nervous spirits.

The cerebral mechanism is protected by the bony skull, internal to which the hard outer meninx (*dura mater*) serves to "restrain and keep within the brain the effluvia's of the animal spirits, lest they should too thickly evaporatore," and thus be dissipated to the great detriment of the body. This heavy meninx is important also in containing capacious cavities ("bosoms" in Willis' terminology), which, "like promptuaries or store houses framed in several places," receive the blood returning from every portion of the brain, finally transferring their contents to the jugular veins. These sinus-like enlargements are, however, more than storage depots; they, too, are auxiliary refineries, since, while the blood remains

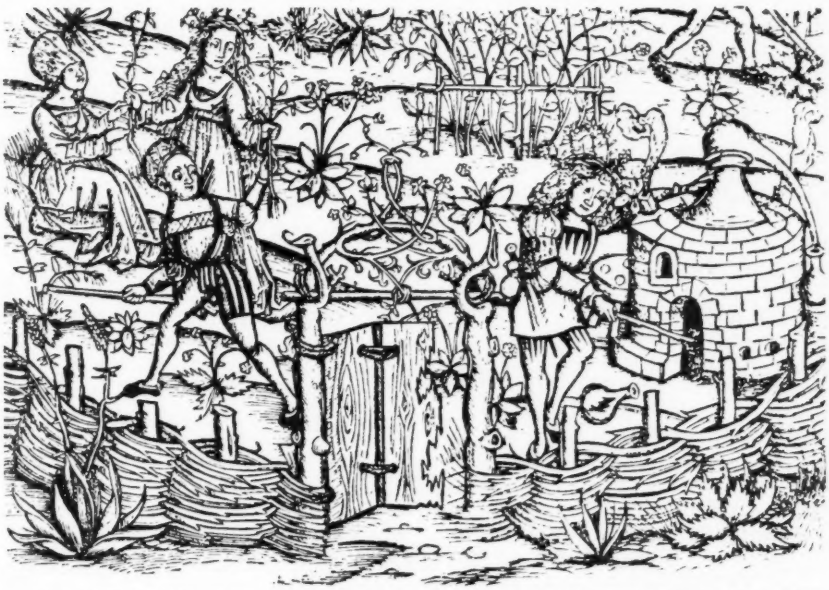


Fig. 7. Ancient distillation. From *Pictorial History of Ancient Pharmacy*, by Hermann Peters, translation by Wm. Netter, Chicago, G. P. Engelhard Co., 1889.

collected within them, it seems to be the source of heat, "requisite for the distilling forth of the animal spirits, as if it were a certain chymical reaction." These bosoms, then, "are like a certain distillatory bath; so the other membrane of the dura mater, being stretched out about the whole head, is like an impervious alembick, which with its covering keeps within the spirituous breaths, that they not be immoderately evaporated." In this way, by admirable contrivance, heat is engendered in the localized furnaces, and is conserved by dural and osseous insulation.

The interior soft meninx, far thinner than the exterior, is "covered over throughout with the infoldings of arteries and veins . . . and so waters all the spaces of the brain and cerebel with unnumerable rivers." Then these arteries and veins meet in anastomoses, in order that "the blood to be carried from the heart into divers regions of the brain, might be exactly mingled as to its parts and particles, before it come to the place designed." They are multiple in order that, "if by chance one or two should be stopt, there might easily be found another passage instead of them."

Thus it is that the meningeal and cerebral vessels which carry the vapors through the whole compass of the head are like distillatory organs. The latter, in the process of cephalic circulation, separate the purer and more active particles from the rest, subtilize them, and finally insinuate the spiritualized elements into the substance of the brain. The spiritous distillate, regardless of what its destination may be, must first be absorbed in this fashion by the brain tissue; to that end "its whole exterior superficies is made uneven and broken, with turnings and windings and rollings about, almost like those of the intestines"; thus, with a complex pattern of gyri and sulci, it is "framed both for the more plentiful reception of the spirituous aliment, and also for the more commoding dispensation of the animal spirits"; this nutrient spirit is "not only drunk in everywhere in the plain superficies," but also through the walls of the sulci, the folds being so disposed in order that "the spaces for the receiving the juyce might be enlarged."

These animal spirits, derived from the spirituous liquor, are carried into the callous body, "as into a spacious field." The corpus callosum (Fig. 2c, at *K*), according to Willis, is the headquarters of the animal faculties, there residing "as in a publick emporium or mart"; from this repository, as occasion serves, "they are raised up, and drawn forth for the uses of every faculty." While at relative leisure, they gently circulate through the corpus callosum and spread to the fornix. In

musing or reveries, the streaked pathways of the fornix are their sheltered lanes; along these are engendered our sorrows and sighs, our joys and smiles.

At regular intervals the cerebral tissue becomes surfeited with its spiritous content; flowing inwardly it "stuffs all the pores and passages of the brain, and so excludes for that time the spirits from wonted tracts and orbs of expansion"; whereupon, "sleep, or an eclipse of the animal spirits happens." Conversely, "waking returns, when from the liquor instilled, the more subtil part is exalted into very pure spirits, and at length the more watry, being partly resolved into vapours, is exhaled, and partly supped up by the passages entring the substance of the brain."

This discussion of storage introduces the matter of the cerebral ventricles, for which a use is found in the traditional manner.

The presence of the ventricular spaces had brought pacific pleasure to the philosophers of the early Church. Albert Magnus, the learned Dominican, depicted them in stylized fashion (Fig. 4b); they offered a sheltered nidus for the soul, a place for ultimate refinement of a spirit whose source was celestial. By Gregor Reisch, Confessor of Emperor Maximilian I, they were compartmentalized, to care for the activities of imagination, cogitation, fantasy, memory and the kindred forms of cerebration. In Peyligk's medieval compendium for lay scholars, the ventricles took the traditional form (Fig. 4a) to subserve the familiar philosophic function. And, although the anatomy of the scalp and cranium was pictured with structural correctness by Dryander, the ventricles were superimposed upon the calvarium in stereotyped treatment (Fig. 4c). Willis must fit these cavities into his schema, "since there is nothing met with in Nature that is not destinated to some use." But he modifies the inherited system to meet his needs. In Willis' opinion the serous latex, which is the vehicle of the spirits, and is introduced together with them into the pores of the brain, "after it is grown stale, and being attenuated into vapour, doth distill forth into this cavern, and there at last grows into a watry humor." The humor, having served its purpose as a vehicle, is then removed by the veins—as if it were a condensation falling into the cucurbite.

The discussion then passes from the brain to the "spinal marrow." In form it is "forked, as it were like the poets Parnassus, like the letter Y" (Fig. 2d). Because of the relative directness of its course from head to tail, and because of the simplicity of its structure, "the oblong marrow seems to be a broad or high road, into which all the animal spirits perpetually flow from their double fountain to wit the brain and cerebel, to be derived from thence into all the nervous parts of the whole body." From the cephalic stations the animal spirits are "directed either outward towards the nerves, when they exert the locomotive faculty or they look inward towards their fountains, when the acts of sense, or rather the apprehensions of sensible things are performed." Within the oblong marrow "a more large and greatly open path leads straight to the spinal marrow, through which the spirits flow forth to the nerves, the executors of spontaneous motion in most members."

The cerebellum possesses a characteristic morphology, and is designed "for some works and wholly distinct from the brain." While within the brain "imagination, memory, discourse, and other more superior acts of the animal function are performed," it is the office of the cerebellum to supply the animal spirits to those nerves by which the involuntary actions (such as cardiac action, respiration, and digestion) are carried out "after a constant manner unknown to us, or whether we will or no." And while we may be aware of the movement of spirits in the cerebrum, those which inhabit the cerebellum "perform unperceivedly and silently their works of nature without our knowledge or care." The difference in spiritous behavior is a consequence of observable structural characters (Fig. 2b); for, "whilst the brain is garnished as it were with uncertain meanders and crankling turnings and windings about," the cerebellum "is furnished with folds and lappets disposed in an orderly series." Within the cerebellum, then, "the animal spirits are expanded according to the rule and method naturally impressed on them . . . as it were in a certain artificial machine or clock," not as the same spirits are regimented in the cerebrum, where they are "continually driven into fluctuations as it were with the winds of passions and cogitations." From the cerebellum the oblong marrow is continued "into the utmost recesses of the whole spine or backbone." This medullary prolongation, the spinal marrow, "is as it were the common passage or chanel of the spirits flowing out of the head into the nerves." They follow the nervous pathways to the muscles, return by them from the organs of sense. The swellings at the brachial and the lumbosacral levels resemble, according to Willis, the widenings which occur in a channel where rivulets are received.

Thus Thomas Willis succeeded in utilizing all the gross anatomical eminences, gyrate ridges, arches, vessels and investments found within the cranial cavity; in this investigation he was un-

aided by experimentation or staining procedure.[7] Willis' anatomical studies carried him far in the field of gross morphology; he presented the fourfold arterial supply and dural venous reservoirs in the detailed manner now made familiar to all students by our modern encyclopedic textbooks; the chief macroscopic features of the cerebrum, cerebellum, medulla oblongata, and spinal cord were accounted for in his treatise. However, in zealously attempting to discover a use for each dilated vascular channel, laminated prominence, ventricular space, foramen, and medullary rootlet, he was drawn into fallacious physiologic interpretations. Thomas Willis progressed as far in the field of functional interpretation as the ancient, and astonishingly persistent, system of physiology would allow. Thinking only in terms of the transmission or of the temporary warehousing of the spiritus, Doctor Willis sought in each discrete anatomic structure a suitable headquarters for a vaporous distillate; striation gave evidence of the existence of minute tubules, not of the presence of nerve-fibers; nuclear bulging indicated a massing of spongious substance, not the grouping of cell-bodies. Influenced profoundly by the inherited medical beliefs of his own and of past centuries, Willis assigned a chemical function to the heated blood, the meningeal vessels, the dural shroud, and the cranial vault. They represented parts of a human balneum Mariae. Willis, reasoning that whatever refining process was serviceable in the preparation of a medicine must be infinitely more important in the purification of a vapor which is destined to become the soul of man, did not hesitate to put into the cranial cavity the neural counterparts of an apothecary's paraphernalia. The *Cerebre Anatome*, therefore, bridges the gap between the sixteenth century, Vesalian, neuro-anatomy and that of our own day; with interpretative resourcefulness and ingenious logic it fits new anatomic pieces into a predetermined physiologic pattern.

It must be remembered that Willis was limited by the power of gross observation; his knowledge was gained solely by dissection. No one had seen the cellular constituents of a nuclear mass, the fibrillar content of a neural tract, the histologic elements of bark and pith of cerebral and cerebellar cortices. Spaces were interpreted as reservoirs to receive, cleanse, store and dispense the spiritus; laminar walls were serried tracks for the guided

[7] A correct interpretation of cerebral and cerebellar function must wait, of course, upon a clear demonstration of the tracts; even the pioneers of modern neurology presented their discoveries as late as the nineteenth century; in the sixty years between 1819 and 1879, Burdach, Goll Gowers, Clarke and Flechig described the tracts, fascicles or columns which bear their names.

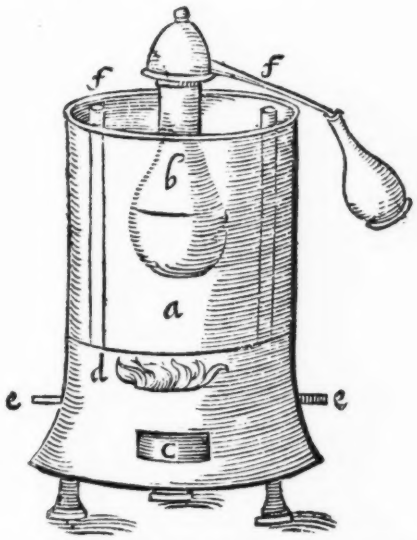


Fig. 8. Distillation in Balneum Mariae. a, Copper vessel full of water; b, Gourd-shaped flask, or cucurbite, containing the material to be distilled; c, Door through which a lamp is placed, then closed; d, Oil lamp, with three or four wicks, beneath the vessel; e, Openings through which air enters; f, Two pipes, passing through the water, by which fumes escape. Figure taken from *Antidotarium Generale*, by Johann Jacob Wecker, Basil, 1526; the legend is a translation of Wecker's Latin description.

and enchanneled movement of the same; eminences were manufactories or places for collection of excrementitious wastes—of dregs removed to sanitize the vital fuel; nerves were pervious branches of a medullary tree—whose porosities were arborescent continuations of larger spaces at the core of the brain.

Similarly, Thomas Willis' explication of cardiovascular action is fundamentally Galenic, his notion of arterial content is rooted in Empedoclean and Aristotelian philosophy. Willis adds the "chymical" phenomenon of admixture. While the spirits are the ethereal particles of a divine breathing, sulphur, salt and nitre are of earthly derivation. In the animal body, the several kinds of particles, by fermentation, break apart; the rarefied part, "like Water boyling over a Fire," is carried through the vessels with great tumult and turgency, moved by the vital ferment in the "Chimny of the Heart." In Willis' schema, as in that of the ancient writers, the heart is the important workshop of the blood. Willis adds to the older concepts a description of a mechanism for heating the blood. He believes that it is accom-

plished by an actual flame, fed through an access of air from the outer atmosphere. The flame produces a sooty effluvium, which it is the office of the lungs and the cutaneous pores to remove. The flame which burns in the heart sends the rarefied blood away through all aortic branchings; laying aside, peripherally, its "turgid and burning particles," the blood, now "more quiet and half extinct," and reduced in vigor, returns through the veins for rejuvenation, for rekindling and distribution.

William Harvey proved, by the simple experiment of arteriotomy, that the arteries contain blood and blood alone—not an airy spirit derived in part from the chyliferous mixture in the veins; the heart was clearly described as a muscle, which, growing hard upon contraction, squeezed the contained fluid from the cardiac spaces by parietal contraction. As the charge was sent along its way, from the core of the body to the periphery, thence in a circle backward through the veins into the right side of the heart, the venous valves served to prevent a reflux of the blood. The blood, according to Harvey's concept, moved in accordance with hydrodynamic laws. To Thomas Willis, on the contrary, "blood" is not constantly a liquid, but rather a quintessential vapor driven onward in the form of a jet; the heart is a lamp from whose pipes the subtle part of steams are driven by impulsive rush. To Harvey the cephalic vessels are the unexalted parts of a thoroughly ramifying system; in Willis' scheme, so celestial is cerebral and meningeal structure, and so penetrating and volatile the spirit sent upward from the heart, that he finds it impossible to believe that its ascent and cephalic meandering are accomplished through ordinary vessels; within the brain it is not blood (in the now familiar meaning of the term), but a perfected distillate whose further course will take it through permeable nerves. According to Harvey, the movement of the blood through the general bodily channels was due to muscular mechanism; to Willis, flow is the result of turgency occasioned by heating. To Harvey, blood was a true liquid which brightened when spilled from a vein; to Willis it is a pneumatic fragment of a world-soul. In its Galenic fundamentals Thomas Willis' concept is fourteen centuries old; it is tradition embellished with new physical additions —an ancestral favorite in seventeenth century dress. William Harvey's presentation was as novel as it was bold—based upon experiment and limited to judgment born of observable facts. Thomas Willis reconverts the cardiac "Mansion of the Soul" into a kind of distillery, although William Harvey proved that it was a pump.

There is naught to indicate that Sir Christopher Wren did more than faithfully delineate encephalic anatomy, employing the meticulous technique which characterizes his architectural sketches and drawings. For the Cathedral he prepared many plans, discarding the artistically inappropriate and the mechanically unworkable. For the globous brain, nobly housed within the bony armor of the skull, he seems content to set down careful figures—without questioning the interpretative uses of his friend, Doctor Willis. Perhaps, supported by contradictory evidence gleaned from his own forays into the field of vascular physiology, he remonstrated with Willis; however, there remains no textual evidence of such difference of opinion. For all we know to contrary, Sir Christopher dutifully limited his commission to that of illustrator.

In this statement there should be no reproachful word. However, there might, defensibly, be a mildly opprobrious note in any commentary on Thomas Willis' failure to regard the direct statements in, and the implication of, William Harvey's *Exercitatio* and Richard Lower's *Tractatus*. Doctor Willis' almost complete disregard of cardiac anatomy and of arteriovenous content seems an astonishing instance of scientific insularity. Enamored of a system, Willis composed a treatise which, in coming after Harvey's exercitation, now seems to be anachronistic; the ideas of Willis and of Harvey, if they are viewed as markers in the conceptual progress of medical history, appear to have been reversed fantastically in the order of time.

In the eighth chapter of his *Exercitatio Anatomica*, William Harvey recorded that he was in apprehension for his fate among thinking men. He wrote, "I not only fear injury to myself from the envy of a few, but I tremble lest I have mankind at large for my enemies, so much doth wont and custom, that become as another nature, and doctrine once sown and that hath struck deep root, and respect for antiquity influence all men." Harvey feared outright attack from recalcitrant colleagues—and lived to experience their verbal assault. He had not reckoned with the force of disregard, quietly efficacious in hindering the advance of knowledge. And, in all probability, Harvey had not expected such neglect at the hands of a fellow-member of the Royal Society.

REVIEWS OF NEW BOOKS

THE author of the book entitled *Histopathologic Technic*[1] had certain very definite purposes in mind. It was written to give a systematic treatment of recent advances in this field without attempting to be encyclopedic in scope. Many methods that have been included in previous works on this subject have been excluded either because they are obsolete or impractical or because they have been replaced by better methods. He has endeavored to find methods that depend for constancy of results on controllable factors, such as time, temperature, hydrogen ion concentration, and concentration of reagents rather than upon the skill of the technician. Most of the methods described are applicable to tissues fixed routinely in formalin rather than in special fixatives. The author has, himself, made many modifications and improvements of older methods.

The volume is divided into 21 chapters. The first six chapters deal with the use of the microscope, the equipment essential to histopathologic technique and the general principles of fixation, decalcification, sectioning, and straining. These are followed by chapters dealing with the staining of specific parts of tissues, such as nuclei, cytoplasm, enzymes, pigments, cell products (glycogen, mucin, etc.). fats and lipoids, connective tissue, parasites, and tissue of the nervous system. Chapter 19 describes methods of dealing with hard tissues, such as teeth and bone. Chapter 20 describes various special procedures, such as vascular injection, corrosion, autoradiography, and microincineration. The final chapter deals with buffers, with a description of the principles involved and 5 pages of tables for the making of various buffer solutions.

Of particular importance is the chapter dealing with the demonstration of enzymes in tissue. Methods are described for alkaline and acid phosphatases, lipases, oxidases, and dopa melanase. These are among the more recent significant advances in histopathologic technique.

Directions for staining are clear and arranged in a step-by-step manner. The results of special stains are stated so that differentiated tissue may be readily identified. Of particular interest is the manner of dealing with groups of staining methods for special purposes. For example, on pages 172 and 173 differences in fixation, washing, mordanting, sectioning, staining, counterstaining, etc. of eight different methods of staining myelin (Weigert, Pal, Weil, etc.) are given in tabular form. Table 6 lists the comparative schedules of five methods for iron hematoxylin staining; while in tables 11 and 12 are presented the schedules for various methods of staining reticulum.

References are given for all the methods described and their modifications. The entire volume is well written and anyone who is interested in histologic technique will find it extremely useful.

OPAL E. HEPLER.

IN the strict sense of the word *The Long Walk*[2] by Betsy Barton is not a novel. No central character, no theme of events, no climactic adventure form the axis of the story. Rather, it is a depiction of the routine events and experiences on a ward for men with injuries of the spinal cord in a Veterans' Administration hospital. The passage of a few hours in her story has been sufficient for the author to lay bare with a restrained hand the personal tragedies, frustrations, unfulfilled dreams, and warped philosophies which may be a part of doctors and patients alike.

The story has to do with the mastery of individual fears and conflicts which leads to a happier personal life and a life more useful to others. Woody helped his ward mates by example, but his own cares were resolved only in death. Arthur, the hospital psychologist, was unable to succeed in his own work until he had found the means and strength to heal himself. Henri, unbothered by the usual mental fetters of the paraplegic patient, became truly rehabilitated. Janet, through whom the author speaks autobiographically and therefore knowingly, expresses the long struggle with the emotional adjustment that is necessary before the "outside world" can be risked. For the person of casual interest in the problem of the paraplegic patient this book will do far more toward a clarification of their needs and problems, and especially toward an understanding of their feeling of safety in isolation and of their despair and detachment, than will any amount of mawkishly conceived nonsense on this all too popular subject in current magazines and newspapers.

Fortunately the author has avoided the maudlin —an easy error in treating of her subject. Nor has she shown the injured patient in an all clean, all moral, completely deserving light. She has shown how this admittedly difficult group of patients can render all treatment futile by their own attitude of futility. She has indicated what all discerning doctors know, that is, that if the patient can be helped by his doctors to realize fully the meaning of his condition and to accept it and to take up his life again on a new but by no means hopeless plane, the greatest hurdle will have been passed. Through Janet the reader can learn why the intelligent patient has difficulty in accepting his new, foreshortened world, and through Steve Logan one sees the uselessness of effort which ignorance rebuffs. Do-gooders and other

[1] HISTOPATHOLOGIC TECHNIC. By R. D. Lillie, A.B., M.D. Philadelphia and Toronto: The Blakiston Co., 1948.

[2] THE LONG WALK. Betsy Barton. New York: Duell, Sloan & Pearce, Inc., 1948.

usually poorly informed persons, including many doctors, should read this book.

Many passages will bear close reading and rereading. Some of the prose is excellent. And it is excellent because of its sincerity, directness, and clarity. Brief passages descriptive of little ward events could have been written only by a person both keen and honest. One may feel that with her second book Miss Barton has quietly reached maturity as a writer. JOHN MARTIN.

THE first edition of *The Hospital Care of Neurosurgical Patients*[1] appeared eight years ago, and in that interval it has been popular with internes, residents, and nurses who, it seems, are almost always puzzled by if not in actual fear of the problems of neurosurgical care. The present edition is somewhat enlarged, but yet it does not pass the convenient manual size. Certain additions have been made concerning the relations of the house officer to the patient, the attending surgeon, and other personnel in his own and other departments. There is added a discussion of the use of the antibiotics, developed since the first edition, and the subjects of intervertebral disc protrusion and prefrontal lobotomy are covered briefly but adequately for the purposes of the book. The organization of the book has been improved. Certain minor errors in grammar and terminology are still present in the second edition. The book is written in easy, clear language, and while, as the author states, no attempt has been made to lay down hard and fast rules for neurosurgical care (that varying with the policies of the individual surgeon), yet the basic plan of care as outlined serves as a safe guide for the young physician and the interested nurse. JOHN MARTIN.

THE small book *Physical Treatment of Injuries of the Brain and Allied Nervous Disorders*[2] by K. M. Hern represents the honest efforts of the author, a physical therapist, to apply her own concept of what is basically essential and effective in physical therapy for the patient with a brain injury. Her theme is: "Teach the patient how to do it for himself." She apparently puts little faith in the use of massage, passive exercise, and other standard forms of therapy leading to rehabilitation. So far as the book goes, it shows, by elementary illustrations and English which is almost too simple and informal, some of the steps by which patients can be taught confidence and to carry out co-ordinated movements with their strength which has hitherto been present but misguided. The book gives the impression of being merely a chapter in a larger book on various techniques in physical therapy. There is little that is actually original in it, it is tiresome reading, it does not contain much instruction from page to page because of a repetition of method of instruction, and it is doubted if it will fill any wanted information for well trained American therapists. JOHN MARTIN.

[1] THE HOSPITAL CARE OF NEUROSURGICAL PATIENTS. By Wallace B. Hamby, M.D., F.A.C.S. 2nd ed. Springfield, Illinois: Charles C Thomas, 1948.

[2] PHYSICAL TREATMENT OF INJURIES OF THE BRAIN AND ALLIED NERVOUS DISORDERS. By K. M. Hern. Baltimore: The Williams & Wilkins Co., 1947.

IN the volume, *Identification of Tumors*[3] by Nathan Chandler Foot, a new approach has been used to delineate the pathology of tumors. Before using this text, it is essential to read the preface. Here, the author establishes the basis for his different presentation.

There is a specific aim for simplicity. Controversial matter is eliminated. There is a division into two parts; one, the neoplasms of general distribution and the second the neoplasms of special systems and organs. For some reason tumors of the cardiovascular system are considered in part one. There is a section at the end which may be used to systematize the histologic diagnosis of various new growths. There is a chapter on the technical methods of fixation and staining which, to this reviewer, is unnecessary.

The organization pursues a set pattern: the source, the site, age and sex, gross appearance, microscopic appearance, differential diagnosis, and prognosis. In most instances, there is a photomicrograph in black and white. In general, emphasis is laid upon the microscopic picture.

The major flaw in this entire volume is the use of heterogeneous classifications for the various systems. They must be those of the author. These classifications are confusing to trained pathologists and must be more so to the persons for whom the book was written. Many contain combinations of clinical and pathologic terms to the detriment of both. The outline of breast tumors is particularly distressing and that of the skin is somewhat obsolete.

It is recommended that when this text is revised the classifications be simplified in conjunction with the purpose as defined in the preface and that the sections on technical methods and the tabulations be discarded. With these changes, and even in this present issue, if the factors mentioned are ignored, the book will serve a distinctly useful purpose in acquainting the interested though untrained man in the morphology of human neoplasms.

M. C. WHEELOCK.

TO present in a few paragraphs an adequate appreciation of a volume of 700 pages which represents the results of 30 years of conscientious study, of careful experiment, and of wide clinical experience in the care of surgical infections is the formidable task which faces one in reviewing Meleney's excellent *Treatise on Surgical Infections*.[4] No one familiar with the development of surgical practice during the last quarter of a century but would agree wholeheartedly with Whipple's splendid tribute in the

[3] IDENTIFICATION OF TUMORS: ESSENTIAL GROSS AND MICROSCOPIC PATHOLOGIC FEATURES SYSTEMATICALLY ARRANGED FOR EASIER IDENTIFICATION. By N. Chandler Foot, M.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1948.

[4] TREATISE ON SURGICAL INFECTIONS. By Frank Lamont Meleney, M.D. New York: Oxford University Press, 1948.

introduction "... since Lister's time no surgeon has studied so intensively and has made so many original contributions to the subject of the bacteriology of infection and inflammation requiring surgical therapy as has Dr. Meleney in the past twenty-five years."

The volume opens with a historical chapter on bacterial activity in its relation to life and an account of the slow awakening of men of medicine to the importance of inflammatory disease and the futility of treating it by destructive agents. Hospital gangrene in the Civil War is considered at some length, with quotations from Jones' *Surgical Memoirs of the War of the Rebellion* that describe cases conforming closely to the typical picture of gas gangrene, of rapidly spreading streptococcus infection with gangrene, of bacterial synergistic gangrene, and of chronic undermining ulcer. The two latter conditions, illustrated in color in the frontispiece, are of especial significance because they continued to baffle surgeons for many years after the Civil War and only in recent years was their true character finally recognized and a successful plan of treatment developed as a result of Meleney's long continued bacteriological and experimental studies. The chapter closes with an appreciation of Pasteur and Lister and of their fundamental contributions to surgical science.

In Chapters II, III, and IV, "Surgical Infections and their Classifications," "Sterile Technique," and "Sterilization," the author differentiates "surgical" from "medical" infections, and classifies surgical infections by various criteria—by the final outcome, by the time and manner of outset and, with postoperative infections, by the site or body system chiefly involved. Under "Sterile Technique" the many potential sources of contamination of operative wounds are considered and methods of preventing contamination discussed in detail. The larger part of the 20 pages on "Sterilization" is devoted to the problem of sterilization of air by ultraviolet radiation, of the effects obtained and of the practical applications involved.

Chapter V by Edwin J. Pulaski on "Antisepsis and Disinfection in Relation to Surgical Infections" includes a concise discussion of the mode of action of antiseptics and a comprehensive discussion of the many varieties of antiseptics and disinfectants, beginning with the surface antiseptics and continuing with the dyes, the ammonium compounds, the halogens, the metallic salts, the oxidizing agents, the phenols, and finally the sulfonamides and antibiotics. Though the many antiseptics discussed are not purposefully presented in chronological order of their development or discovery the reader gains a vivid picture of the constant evolution and progress that have come with the passing years in this important phase of surgery.

In Chapters VI and VII on "Infection in Clean Operative Wounds" and "Infection in Accidental Wounds" the author discusses on the basis of his wide personal observations and experience the importance of adequate masking, of careful records, of wound healing and postoperative infection, of the importance of the type of suture material and its complete sterilization, and (in Chapter VII) the results of the studies on the care of wounds and burns made under the direction of the National Research Council during the war years. Though the latter have had wide publicity and evoked much thoughtful discussion many men are still reluctant to accept the thesis that chemotherapeutic agents which are consistently helpful in overcoming spreading infection and which often produce dramatic results when given by mouth or parenterally do not necessarily prevent or control infection when applied locally in contaminated or infected wounds. The explanation, however, becomes increasingly clear in the later chapters which deal with bacterial establishment and spread in the human body.

Miss Balbina Johnson, long an able associate in the Bacteriological Research Laboratory at the Presbyterian Hospital, contributes two important chapters, IX and X,—"The Bacteria That Produce Surgical Infectious Diseases" and "Methods for Bacterial Cultivation." The latter "is not intended to be a complete manual of bacteriologic technics. It represents a résumé of technics that have been used and found satisfactory in the study of surgical infections in the Bacteriological Research Laboratory of the Presbyterian Hospital." How much thought and effort Miss Johnson has brought to her task is evidenced by the fact that Chapter IX is documented by 300 and Chapter X by 41 references to the scientific literature concerned with the history and development of bacteriology. These chapters should serve as a helpful guide and a splendid bibliography for the surgeon seeking light on the bacteriological problems that confront him.

In Chapter XI, "Bacterial Entrance into the Human Body," the author indicates the various potential routes by which bacteria gain a foothold in the tissues—the skin, the respiratory tract, the alimentary tract, etc.—and presents illustrative cases with excellent illustrations of gross specimens and microscopic sections.

In Chapters XII–XVII, "Bacterial Establishment within the Human Body," "Bacterial Spread through the Human Body," "Bacterial Synergism," "Bacterial Antagonism," "The Defense of the Human Body against Bacterial Infection," and "The Mechanism of the Secondary Defenses of the Body" the author presents in a comprehensive fashion the theories and ascertained facts concerning bacteria and their action on inanimate matter and living organisms. Bacterial growth, evolution and metabolism, the production of toxic substances, the manner of bacterial spread with well illustrated examples from case histories, bacterial synergism as exemplified by laboratory studies and clinical examples, the laboratory studies of bacterial and other biological antagonisms that eventually led to the discovery of the now well known antibiotics—all are well presented, with numerous references to the investiga-

tions of the many scientists who have shared in the advances that have been made in the effort to solve the many and baffling problems involved in an understanding of microscopic and ultramicroscopic life and activity.

Chapters XVI and XVII, "The Defense of the Human Body against Bacterial Infection" and "The Mechanism of the Secondary Defenses of the Body" are especially interesting, both because of the historical background presented and the excellent portraits of the men who made outstanding contributions to the study of immunity and because of the clear exposition of the cellular and humoral factors involved in body immunity.

In Chapters XVIII–XXII, "Surgical Principles in the Treatment of Infection," "Chemotherapy in Surgical Infections," "The Treatment of Surgical Infections with Zinc Peroxide," "The Bacteriophage Therapy of Surgical Infections," and "Antibiotic Therapy in Surgical Infections," the author presents a summary of the principles of prevention and treatment of infection as applied in surgical practice today and of the results that have been obtained with the modern weapons at the surgeon's command. Chapter XXII closes with a brief and very modest reference to bacitracin, the antibiotic that was developed in the author's laboratory.

It is only simple truth to say that this comprehensive treatise, so many years in the making, will long serve both as an inspiration and guide to the student and practitioner of surgery. One can be very certain, as Whipple has said, that "only those who have worked with him can understand the time and effort that he has given to these bacteriological studies," and from these efforts the entire surgical profession and the patients for whom they are caring have benefited and will continue to benefit through the coming years. SUMNER L. KOCH.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

PRINCIPI DI CHIRURGIA DEL CERVELLO E DEL MIDOLLO SPINALE. By Africo Serra. Bologna: Licino Cappelli, 1948.

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ESSENTIALS OF PATHOLOGY. By Lawrence W. Smith, M.D., F.C.A.P., and Edwin S. Gault, M.D., F.C.A.P. 3rd ed. Philadelphia and Toronto: The Blakiston Co., 1948.

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OCCUPATIONAL MARKS AND OTHER PHYSICAL SIGNS; A GUIDE TO PERSONAL IDENTIFICATION. By Francesco Ronchese, M.D. New York: Grune & Stratton, 1948.

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MANAGEMENT IN OBSTETRICS. By Andrew M. Claye, M.D. F.R.C.S., F.R.C.O.G. London, New York, Toronto: Geoffrey Cumberlege, Oxford University Press, 1948.

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PLASTER OF PARIS TECHNIC. By Edwin O. Geckeler, M.D. 2nd ed. Baltimore: The Williams & Wilkins Co., 1948.

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THE STORY OF THE JOHNS HOPKINS; FOUR GREAT DOCTORS AND THE MEDICAL SCHOOL THEY CREATED. By Bertram M. Bernheim, M.D. New York and Toronto: Whittlesey House McGraw-Hill Book Co., Inc., 1948.

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